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=> d l126 all tot

L126 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:511030 HCAPLUS
DN 131:161631
TI Medicine for treating **apoptosis** dysfunction containing **oligosaccharides**
IN **Yvin, Jean-claude; Cruz, Florence; Descamps, Valerie; Richard, Christophe; Thibal, Vesna; Arrigo, Patrick; Cloarec, Bernard**
PA Laboratoires **Goemar** S.A., Fr.
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM A61K031-70
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): **1**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9939718	A1	19990812	WO 1999-FR229	19990203 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2774289	A1	19990806	FR 1998-1237	19980203 <--
	AU 9921710	A1	19990823	AU 1999-21710	19990203 <--
	EP 1052996	A1	20001122	EP 1999-901702	19990203 <--
	R: DE, ES, FR, GB, GR, IT, NL, PT				
PRAI	FR 1998-1237	A	19980203 <--		
	WO 1999-FR229	W	19990203 <--		

AB The invention concerns a medicine comprising, as active principle, an

efficient quantity of at least an **oligosaccharide** substance capable of modulating **apoptosis** dysfunction and optionally comprising, on at least some of its unit motifs, at least a substituent of the group comprising sulfate, Me and acetyl groups, the substance being selected from the group comprising: **oligosaccharides** derived by enzymic or chem. process from polymer groups including **.beta. 1-3 glucans** optionally comprising .beta. 1-6 branches; and **oligosaccharides** derived by enzymic or chem. process from **sulfated galactans**, in particular **carrageenan, agar** and porphyrins. Iotacarrageenan was incubated with iotacarrageenase at 45-50.degree. and the hydrolyzed products was ultrafiltered. The efficacy of the above product in prevention of **apoptosis** induced by Fas ligand or anti-Fas receptor antibody was shown.

ST **apoptosis** inhibitor **oligosaccharide carrageenan**

IT **Apoptosis**
(inhibitors; medicine for treating **apoptosis** dysfunction contg. **oligosaccharides**)

IT **Oligosaccharides**, biological studies
Polymers, biological studies
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(medicine for treating **apoptosis** dysfunction contg. **oligosaccharides**)

IT Antibodies
Fas ligand
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(medicine for treating **apoptosis** dysfunction contg. **oligosaccharides**)

IT **Fas antigen**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicine for treating **apoptosis** dysfunction contg. **oligosaccharides**)

IT **9000-07-1, Carrageenan 9002-18-0, Agar 9062-07-1, .iota.-Carrageenan 11016-36-7D, Porphyran**, derivs. **39475-64-4, Galactan sulfate 237069-70-4, .iota.-Neocarratetraose 237069-74-8, .iota.-Neocarrahexaose 237069-76-0, .iota.-Neocarraoctaose 237069-79-3, .iota.-Neocarradecaose 237069-85-1, .iota.-Neocarradodecaose**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(medicine for treating **apoptosis** dysfunction contg. **oligosaccharides**)

RE.CNT 3
RE
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(2) Otsuka Pharmaceutical Co; EP 0552373 A 1993 HCAPLUS
(3) Seikagaku Corp; EP 0795560 A 1997 HCAPLUS

L126 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:774909 HCAPLUS
DN 130:123794
TI CD36 is required for phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or the vitronectin receptor (.alpha.v.beta.3)
AU Fadok, Valerie A.; Warner, Mary L.; Bratton, Donna L.; Henson, Peter M.
CS Dep. Medicine, Pediatrics, National Jewish Medical Res. Center, Denver, CO, 80262, USA
SO J. Immunol. (1998), 161(11), 6250-6257

CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB In vivo, **apoptotic** cells are efficiently removed by professional or nonprofessional phagocytes, a process thought to be essential for tissue remodeling and resoln. of inflammation. Macrophages recognize **apoptotic** cells by several mechanisms, including recognition of exposed phosphatidylserine (PS); however, PS recognition on **apoptotic** cells has not been identified as a feature of human macrophages. The purpose of this study was to detd. whether human monocyte-derived macrophages could be stimulated to recognize PS, defined as inhibition of phagocytosis by PS-contg. liposomes. We also assessed the potential roles for scavenger receptors, CD14, and lectins. Uptake of **apoptotic** neutrophils into unstimulated macrophages was blocked about 50% by Arg-Gly-Asp-Ser and anti-.alpha.v, and up to 20% by oxidized low d. lipoprotein and N-acetylglucosamine, implying a major role for integrin and minor roles of scavenger and lectin receptors. Uptake into macrophages stimulated with **.beta.-1,3-glucan** was blocked 50% by PS liposomes and 40% b y oxidized low d. lipoprotein, suggesting that the macrophages had switched from using integrin to recognition of PS. MEM-18 and 61D3 (anti-CD14 mAbs) were poor inhibitors of **apoptotic** neutrophil uptake, but good inhibitors of **apoptotic** lymphocyte uptake. The switch to PS recognition was accompanied by down-regulation of .alpha.v.beta.3 expression and function. Anti-CD36 blocked uptake into unstimulated or stimulated macrophages, suggesting CD36 involvement not only with the .alpha.v.beta.3 integrin mechanism (as previously reported) but also with PS recognition. A max. of 70% inhibition was achieved by combining anti-CD36 with either anti-av or PS liposomes.
ST CD36 macrophage phagocytosis phosphatidylserine receptor; vitronectin receptor CD36 macrophage phagocytosis
IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(phosphatidylserine; requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)
IT **Apoptosis**
Lymphocyte
Macrophage
Neutrophil
Phagocytosis
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)
IT CD36 (antigen)
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)
IT CD14 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)
IT Integrin .alpha.v.beta.3
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)
IT Lectins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(requirement of CD36 in phagocytosis of **apoptotic** cells by

human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)

IT Phosphatidylserines
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)

IT Scavenger receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(requirement of CD36 in phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or vitronectin receptor (.alpha.v.beta.3) and the role of other receptors)

RE.CNT 49

RE

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L126 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:569434 HCAPLUS
DN 129:270273
TI Ligand binding to the (1.fwdarw.3)-.beta.-D-glucan receptor stimulates NF.kappa.B activation, but not **apoptosis** in U937 cells
AU Battle, James; Ha, Tuanzhu; Li, Chaunfu; Della Beffa, Vittorio; Rice, Peter; Kalbfleisch, John; Browder, William; Williams, David
CS Immunopharmacology Research Group, Department of Surgery, East Tennessee State University, Johnson City, TN, 37614-0575, USA
SO Biochem. Biophys. Res. Commun. (1998), 249(2), 499-504
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
CC 1-7 (Pharmacology)
AB Recent data suggest that sepsis stimulates macrophage **apoptosis** (Ao) with subsequent induction of macrophage dysfunction. Nuclear factor-kappaB (NF.kappa.B) activation has been linked to Ao in either a pro- or antiapoptotic role. Glucans are biol. response modifiers which exert antisepsis activity. This investigation examd. the effect of (1.fwdarw.3)-.beta.-D-glucan receptor binding by a high affinity ligand on Ao and NF.kappa.B activation in U937 cells in the presence or absence of LPS. A high affinity glucan ligand (IC50 = 23 nM) activated NF.kappa.B, but did not induce Ao or significantly alter LPS induced U937 Ao. These data indicate that: (i) modulation of the macrophage (1.fwdarw.3)-.beta.-D-glucan receptor stimulates NF.kappa.B; (ii) does not induce Ao or significantly diminish LPS induced Ao and (iii) activation of the U937 FAS receptor does not alter the relative Ao responses in glucan and LPS treated cells. (c) 1998 Academic Press.
ST glucan receptor ligand sepsis macrophage **apoptosis**
IT **Apoptosis**
Macrophage
Sepsis
(ligand binding to the (1 .fwdarw. 3)-.beta.-D-glucan receptor stimulates NF.kappa.B activation, but not **apoptosis** in U937 cells)
IT NF-.kappa.B
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ligand binding to the (1 .fwdarw. 3)-.beta.-D-glucan receptor stimulates NF.kappa.B activation, but not **apoptosis** in U937 cells)
IT 39464-87-4, Scleroglucan
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(ligand binding to the (1 .fwdarw. 3)-.beta.-D-glucan receptor stimulates NF.kappa.B activation, but not **apoptosis** in U937 cells)
IT **9051-97-2**, (1 .fwdarw. 3)-.beta.-D-Glucan
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand binding to the (1 .fwdarw. 3)-.beta.-D-glucan receptor stimulates NF.kappa.B activation, but not **apoptosis** in U937 cells)

L126 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:60983 HCAPLUS
DN 128:188387
TI Cytotoxic effect against HeLa cells of polysaccharides from the lichen Ramalina celastri
AU Leao, A. M. A. Carneiro; Buchi, D. Freitas; Iacomini, M.; Gorin, P. A. J.; Oliveira, M. B. M.
CS Department of Animal Morphology and Physiology, Federal Rural University of Pernambuco, Recife, Brazil
SO J. Submicrosc. Cytol. Pathol. (1997), 29(4), 503-509
CODEN: JSCPEE; ISSN: 1122-9497
PB Editrice Compositori
DT Journal

LA English
CC 1-6 (Pharmacology)
AB The most active polysaccharides which show antitumoral activity are (1.fwdarw.3)-.beta.-D-glucans, branched or not at O-6. Since these structures are sometimes poorly sol. in aq. media, .alpha.-D-glucans and their chem. derivs., which are more sol., were also studied. The present object is to observe morphol. alterations in HeLa cells caused by two different polysaccharides obtained from the lichen Ramalina celastri, which are (1.fwdarw.3), (1.fwdarw.4)-linked .alpha.-D-glucan and its sulfated deriv. The cells were incubated in Eagle's medium in the absence or presence of each polysaccharide and routinely processed and analyzed by light and electron microscopy. Even though the .alpha.-D-glucan altered the cellular vol., cytoplasmic densities, and mitosis, the resulting monolayer was similar to the control. TEM anal. showed cytoplasmic blebbing and the presence of an amorphous electron-dense material free in the cytoplasm and interior membranes. The enhanced injury caused by the sulfated deriv. was apparent, altering cell adhesion and causing cell aggregation. Nuclear modifications such as fragmentation and condensation of chromatin under the nuclear envelope, which showed to be convoluted, suggested the occurrence of **cell death** by **apoptosis**.
ST antitumor polysaccharide lichen Ramalina
IT Antitumor agents
Apoptosis
Cytotoxic agents
Ramalina celastri
(cytotoxic effect against HeLa cells of polysaccharides from the lichen Ramalina celastri)
IT Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cytotoxic effect against HeLa cells of polysaccharides from the lichen Ramalina celastri)
IT **9051-97-2DP**, (1.fwdarw.3)-.beta.-D-Glucan, derivs.
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(cytotoxic effect against HeLa cells of polysaccharides from the lichen Ramalina celastri)

L126 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:394881 HCAPLUS
DN 125:56189
TI Macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis**
AU Sveinbjoernsson, Baldur; Olsen, Randi; Seternes, Ole M.; Seljelid, Rolf
CS Inst. Med. Biol., Univ. Tromsoe, Tromsoe, N-9037, Norway
SO Biochem. Biophys. Res. Commun. (1996), 223(3), 643-649
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB We have studied the cytotoxic effect of stimulated macrophages on Meth A tumor cells in vitro. When stimulated with interferon-.gamma. and sol. .**beta.-1,3-D-glucan**, macrophages exerted cytotoxicity towards syngeneic Meth A tumor cells. This cytotoxicity was assocd. with a high level of nitric oxide prodn. Both **cell death** and nitric oxide prodn. were significantly inhibited by the addn. of aminoguanidine, a specific inhibitor of inducible nitric oxide synthase (iNOS), to the culture medium. The cytotoxic effect was accompanied by internucleosomal cleavage of DNA as shown by electrophoresis and DNA fragmentation assay.
ST macrophage cytotoxicity sarcoma nitric oxide **apoptosis**
IT Deoxyribonucleic acids
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cleavage; macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis** and)

IT **Apoptosis**
Macrophage
Sarcoma
(macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis**)
IT Interferons
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(.gamma., macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis** and)
IT 10102-43-9, Nitric oxide, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis**)
IT **9051-97-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(macrophage cytotoxicity against murine Meth A sarcoma involves nitric oxide-mediated **apoptosis** and)

L126 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:742064 HCAPLUS
DN 123:132275
TI Modulation of the **antitumor** effect and tissue distribution of highly **branched** (1.fwdarw.3)-.**beta**.-D-**glucan**, **SSG**, by **carrageenan**
AU Suda, Masahiro; Ohno, Naohito; Adachi, Yoshiyuki; Yadomae, Toshiro
CS Laboratory of Immunopharmacology of Microbial Products, Tokyo University of Pharmacy and Life Science, Tokyo, 192-03, Japan
SO Biol. Pharm. Bull. (**1995**), 18(5), 772-5
CODEN: BPBLEO; ISSN: 0918-6158
DT Journal
LA English
CC **1-6** (Pharmacology)
AB The action of **carrageenan** (CAR), a representative blocking reagent for phagocytes, on the antitumor effect and tissue distribution of highly branched (1.fwdarw.3)-.**beta**.-D-**glucan**, SSG, was examd. CAR inhibited the antitumor effect of i.p. administered SSG only when applied before inoculation of the tumor, and had little effect when applied after tumor inoculation. A similar result was obsd. when SSG was administered intralesionally. In contrast, CAR had considerable effect on tissue distribution of i.p. SSG. The differences with respect to the results in normal mice were: (1) the distribution of SSG from the peritoneal cavity to the rest of the body was inhibited, (2) large nos. of peritoneal exudate cells (PEC) were produced and a relatively high concn. of 3H-SSG was found in the PEC fraction 48 h after administration of 3H-SSG, (3) one week after administration, 3H-SSG was distributed to throughout the body but the amt. of 3H-SSG distributed was lower than in normal mice, (4) a significant amt. of 3H-SSG was recovered from ligaments (contg. omental milky spots, peritoneum, mesentery and assocd. fat) in which negligible amts. were found in normal mice. These results suggest that the inhibition of the antitumor effect of SSG by CAR probably results from the prevention of the natural resistance of mice which is related to phagocytic function, and that the distribution of SSG to throughout the body is significantly modulated by CAR.
ST SSG antitumor activity tissue distribution **carrageenan**
IT Animal tissue
Neoplasm inhibitors
(**carrageenan** modulation of antitumor effect and tissue distribution of SSG)
IT Neoplasm inhibitors
(sarcoma, **carrageenan** modulation of antitumor effect and tissue distribution of SSG)
IT **9000-07-1, Carrageenan**
RL: BAC (Biological activity or effector, except adverse); BIOL

(Biological study)
(**carrageenan** modulation of antitumor effect and tissue distribution of SSG)

IT **9051-97-2**, SSG
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**carrageenan** modulation of antitumor effect and tissue distribution of SSG)

L126 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1988:209 HCAPLUS
DN 108:209
TI **Antitumor** activity of a highly **branched** (1 .fwdarw. 3)-.**beta**.-D-**glucan**, **SSG**, obtained from Sclerotinia sclerotiorum IFO 9395
AU Ohno, Naohito; Kurachi, Kazuya; Yadomae, Toshiro
CS Tokyo Coll. Pharm., Hachioji, 192-03, Japan
SO J. Pharmacobio-Dyn. (**1987**), 10(9), 478-86
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
CC **1-3** (Pharmacology)
Section cross-reference(s): 33
AB The antitumor activity of a highly branched (1.fwdarw.3)-.**beta**.-D-**glucan**, SSG, purified from the liq. culture filtrate of S. sclerotiorum IFO 9395 and its several derivs. were tested in ICR mice bearing Sarcoma 180 cells. SSG was effective by both systemic (i.p. and i.v.) and local (intratumoral) administrations on the solid form of Sarcoma 180 in ICR mice and the mice acquired resistance to subsequent inoculation of Sarcoma 180. However, SSG was not effective on the ascites from Sarcoma 180. The pretreatment of ICR mice with **carrageenan** suppressed the antitumor activity, suggesting the involvement of macrophages on the antitumor activity. Derivs. prepd. from SSG by periodate oxidn./borohydride redn. showed antitumor activity, but those obtained after acetylation, carboxymethylation and hydroxyethylation were less active. Apparently, SSG is a useful antitumor glucan which modifies biol. responses and can be used as a source for some antitumor derivs.
ST Sclerotinia glucan antitumor
IT Macrophage
(in neoplasm inhibition by Sclerotinia sclerotiorum glucan derivs.)
IT Neoplasm inhibitors
(Sclerotinia sclerotiorum glucan derivs. as, prepn. of and structure in relation to)
IT Molecular structure-biological activity relationship
(neoplasm-inhibiting, of Sclerotinia sclerotiorum glucan derivs.)
IT 53238-80-5
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of, structure in relation to)
IT 53238-80-5DP, oxidized and reduced 111854-08-1P 111854-09-2P 111854-10-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and neoplasm-inhibiting activity of, structure in relation to)

L126 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:596356 HCAPLUS
DN 107:196356
TI Tumor cytotoxicity of polymorphonuclear leukocytes in beige mice: linkage of high responsiveness to linear .**beta**.-**1,3**-D-**glucan** with the beige gene
AU Fukase, Shigeru; Inoue, Tomio; Arai, Shigeru; Sendo, Fujiro
CS Sch. Med., Yamagata Univ., Yamagata, 990-23, Japan
SO Cancer Res. (1987), 47(18), 4842-7
CODEN: CNREA8; ISSN: 0008-5472

DT Journal
LA English
CC 15-10 (Immunochemistry)
Section cross-reference(s): 3
AB Beige mice (bg/bg) have many functional defects in their leukocytes and these phenotypes are inherited in an autosomal recessive manner. The tumor cytotoxicity of polymorphonuclear leukocytes (PMN) obtained from bg/bg was studied. The intensity of tumor cytotoxicity of PMN induced by linear **.beta.-1,3-D-glucan** was higher in bg/bg PMN than in PMN of heterozygous control mice (bg/+). To analyze this phenomenon more precisely from the genetic viewpoint, the tumor cytotoxicity of PMN from mice obtained by several mating expts. was detd. The intensity of linear **.beta.-1,3-D-glucan**-induced PMN cytotoxicity was genetically defined and linked completely with the beige gene. In litter mates obtained from cross mating, PMN from only bg/bg showed higher tumor cytotoxicity than those from bg/+ or mice that do not possess the beige gene (+/+). Tumor cytotoxicity induced by other stimulants (phorbol myristate acetate and cytokines) was not higher in bg/bg than bg/+ or +/+ PMN. Thus, the high responsiveness to linear **.beta.-1,3-D-glucan** in terms of tumor cytotoxicity of PMN was deted. by the locus that is linked to the beige gene and is expressed in an autosomal recessive manner.
ST tumor cytotoxicity polymorphonuclear leukocyte beige mouse; gene linkage beige glucan response
IT Neoplasm
(**cytolysis** of, by glucan-responsive polymorphonuclear leukocyte, in beige mouse)
IT **Cytolysis**
(of neoplasm, by glucan-responsive polymorphonuclear leukocyte, in beige mouse)
IT Mouse
(tumor cytotoxicity of glucan-responsive polymorphonuclear leukocyte in beige, gene linkage in)
IT Leukocyte
(polymorphonuclear, glucan responsiveness and tumor cytotoxicity of, in beige mouse, gene linkage in)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(bg, linkage of gene for glucan-responsive polymorphonuclear leukocyte and, of beige mouse)
IT 9051-97-2
RL: BIOL (Biological study)
(linear, polymorphonuclear leukocyte responsiveness to, gene linkage in beige mouse with)

L126 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:405547 HCAPLUS
DN 107:5547
TI Macrophage stimulation with some structurally related polysaccharides
AU Artursson, Per; Edman, P.; Ericsson, J. L. E.
CS Biomed. Cent., Univ. Uppsala, Uppsala, S-75125, Swed.
SO Scand. J. Immunol. (1987), 25(3), 245-54
CODEN: SJIMAX; ISSN: 0300-9475
DT Journal
LA English
CC 15-10 (Immunochemistry)
Section cross-reference(s): 63
AB The macrophage-stimulating properties of some structurally related polysaccharides were studied in vitro. When the polysaccharides were presented to the macrophages in a sterically fixed form, i.e. as microparticles, they induced the release of interleukin 1 (IL-1) from the macrophages. Microparticulate **1,3-.beta.-glucan** (curdlan) nonspecific macrophage mediated tumor cell killing while 1,4-.alpha.-glucan (starch), 1,6-.alpha.-glucan (dextran), and 1,6-.alpha.-mannan were without effect. The corresponding sol.

polysaccharides did not stimulate the macrophages. Kinetic studies showed that although IL-1 was released immediately after stimulation, the macrophages needed a time lag of several days to develop tumor cytotoxicity. The development of cytotoxicity paralleled binding of tumor cells to the macrophages. Resident and inflammatory peritoneal macrophages showed differences in their responses to the polysaccharides. Stationary, resident peritoneal macrophages stimulated by macroparticles secreted high levels of IL-1 but expressed a low cytotoxic activity, while newly recruited inflammatory macrophages released lower levels of IL-1 but readily killed the tumor cells. The influence of cyclooxygenase products on the IL-1 release and macrophage cytotoxicity was also investigated. When cyclooxygenase was blocked with indomethacin, a significantly higher release of IL-1, and then an increased cytotoxicity, were obtained with **1.3-.beta.-glucan** stimulated macrophages. Thus, microparticulate polysaccharides may be useful for studies on the induction of macrophage differentiation and also for studies on nonspecific cellular immune responses in vitro and in vivo.

ST macrophage stimulation polysaccharide; microparticle polysaccharide macrophage stimulation

IT **Cytolysis**
(by macrophage, polysaccharide microparticles stimulation of)

IT Macrophage
(**cytolytic** activity of, interleukin 1 release by, polysaccharide microparticles stimulation of)

IT Polysaccharides, biological studies
RL: BIOL (Biological study)
(acryloyl, microparticles, macrophage stimulated by, **cytolytic** activity of and interleukin 1 release by)

IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(interleukin 1, formation of, by macrophage, polysaccharide microparticles stimulation of)

IT Pharmaceutical dosage forms
(microparticles, acryloylated polysaccharide, macrophage stimulated by, **cytolytic** activity of and interleukin 1 release by)

IT 39316-65-9 63653-15-6 108598-47-6 108598-84-1
RL: BIOL (Biological study)
(microparticles, macrophage stimulated by, **cytolytic** activity of and interleukin 1 release by)

L126 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:202431 HCAPLUS
DN 102:202431
TI A soluble **.beta.-1,3-D-glucan** derivative potentiates the cytostatic and **cytolytic** capacity of mouse peritoneal macrophages in vitro
AU Seljelid, Rolf; Boegwald, Jarl; Hoffman, James; Larm, Olle
CS Inst. Med. Biol., Univ. Tromso, Tromso, N-9001, Norway
SO Immunopharmacology (1984), 7(1), 69-73
CODEN: IMMUDP; ISSN: 0162-3109
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB An aminated **.beta.-1,3-D-glucan** deriv., curdlan, is reported to render macrophages cytostatic to L-929 cells and to potentiate macrophage cytotoxicity to the tumor cells in vitro.
ST curdlan glucan deriv tumor **cytolysis** macrophage
IT Neoplasm inhibitors
(curdlan as, macrophage in relation to)
IT **Cytolysis**
(of neoplasm, by peritoneal macrophage, enhancement of, by activated curdlan)
IT Macrophage
(tumor **cytolysis** and cytostasis by, potentiation of, by activated curdlan)

IT 54724-00-4
RL: BIOL (Biological study)
(tumor inhibition by macrophage enhancement by)

L126 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:400346 HCAPLUS
DN 101:346
TI Early cellular responses in the peritoneal cavity of mice to **antitumor** immunomodulators
AU Morikawa, Kaoru; Kikuchi, Yoshiaki; Abe, Shigeru; Yamazaki, Masatoshi; Mizuno, Denichi
CS Fac. Pharm. Sci., Teikyo Univ., Kanagawa, 199-01, Japan
SO Gann (**1984**), 75(4), 370-8
CODEN: GANNA2; ISSN: 0016-450X
DT Journal
LA English
CC **1-6** (Pharmacology)
AB The early cellular responses to antitumor immunomodulators and conventional inducers, esp. the polymorphonuclear leukocyte (PMN) responses, were examd. in the peritoneal cavity of mice to investigate their effect on primary defense mechanisms. Immunomodulators were classified into 5 groups in terms of PMN response on the basis of its duration (declining or persistent) and extent (high or low induction): 1) TAK (.**beta.**-**1,3-glucan**)-type (high, persistent), 2) lentinan-type (high, declining), 3) yeast mannan-type (low, declining), 4) LPS (lipopolysaccharide)-type (low, persistent), 5) others (no effect). Since the general PMN response is of the declining type, the persistence of PMN with TAK- and LPS-type immunomodulators is a characteristic of the PMN-inducing activity. TAK- and lentinan-type immunomodulators induced larger nos. of PMN and macrophages than conventional inducers. Thus, some types of immunomodulators have effects on the early host-defense mechanism.
ST peritoneal cavity cell antitumor immunomodulator; leukocyte polymorphonuclear antitumor immunomodulator
IT Macrophage
(antitumor immunomodulators and conventional inducers effect on, antitumor mechanism in relation to)
IT Neoplasm inhibitors
(immunomodulators, cellular response in peritoneal cavity to)
IT Caseins, biological studies
Lipopolysaccharides
Polysaccharides, biological studies
RL: BIOL (Biological study)
(macrophage and polymorphonuclear leukocyte in peritoneal cavity response to)
IT Immunity
(modulators of, antitumor mechanism of)
IT Leukocyte
(polymorphonuclear, antitumor immunomodulators and conventional inducers effect on, antitumor mechanism in relation to)
IT 68-11-1, biological studies **9000-07-1** 9004-54-0, biological studies 9005-79-2, biological studies 9036-88-8 **9051-97-2** 11028-71-0 14769-73-4 24939-03-5 37339-90-5 39325-01-4 53678-77-6 61163-25-5
RL: BIOL (Biological study)
(macrophage and polymorphonuclear leukocyte in peritoneal cavity response to)

L126 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1982:607775 HCAPLUS
DN 97:207775
TI Polysaccharides in **fungi**. Part XI. Antiinflammatory activity and **conformational** behavior of a **branched** (1 .fwdarw. 3)-.**beta.**-D-**glucan** from an alkaline extract of Dictyophora indusiata Fisch
AU Hara, Chihiro; Kiho, Tadashi; Tanaka, Yushiro; Ukai, Shigeo

CS Gifu Coll. Pharm., Gifu, 502, Japan
SO Carbohydr. Res. (**1982**), 110(1), 77-87
CODEN: CRBRAT; ISSN: 0008-6215
DT Journal
LA English
CC **1-3** (Pharmacology)
AB T-5-N [53238-80-5], A (1.fwdarw.6)-branched (1.fwdarw.3)-.**beta**.-D-**glucan** isolated from a M NaOH ext. of the fruit bodies of D. indusiata markedly exhibited antiinflammatory effects on both **carrageenan**-induced edema and scalded edematous hyperalgesia in rat hindpaws. The activities of T-5-N (25 mg/kg i.p. .times. 2) were more potent than those of phenylbutazone (25-50 mg/kg i.p. .times. 2). The conformational behavior of T-5-N was studied. Its mol. wt. in neutral soln. was about three times that in 0.25M NaOH. This finding, in addn. to the results of optical rotatory measurement and complex-formation with Congo Red, indicated that T-5-N has an ordered, triple-helical structure in neutral or slightly alk. soln. (<0.15M NaOH), and has single chains in highly alk. soln. (>0.25M NaOH). The conformational transition occurs at concns. of NaOH in the range of 0.15-0.25 M.
ST T5N conformation antiinflammatory; structure activity T5N; glucan conformation antiinflammatory
IT Inflammation inhibitors and Antiarthritics
(glucans as, structure in relation to)
IT Conformation and Conformers
(of glucan)
IT Molecular structure-biological activity relationship
(inflammation-inhibiting, of glucans)
IT 53238-80-5
RL: BIOL (Biological study)
(conformation and inflammation-inhibiting activity of)
IT **9051-97-2D**, (1.fwdarw.6)-branched derivs.
RL: BIOL (Biological study)
(inflammation-inhibiting activity of, structure in relation to)

L126 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1982:193044 HCAPLUS
DN 96:193044
TI Host-mediated **antitumor** polysaccharides. III. Fractionation, chemical structure, and **antitumor** activity of water-soluble homoglucans isolated from kofukisarunokoshikake, the fruit body of Ganoderma applanatum
AU Mizuno, Takashi; Hayashi, Katsuyuki; Arakawa, Masao; Shinkai, Kenkichi; Shimizu, Masako; Tanaka, Motohiro
CS Fac. Agric., Shizuoka Univ., Shizuoka, Japan
SO Shizuoka Daigaku Nogakubu Kenkyu Hokoku (**1981**), (31), 49-64
CODEN: SDNKAA; ISSN: 0559-8850
DT Journal
LA Japanese
CC **1-6** (Pharmacology)
AB The polysaccharides in the fruit body of G. applanatum were composed of hemicelluloses 33.1%, cellulose 14.4%, pectic substances 1.5%, 50% EtOH-sol. polysaccharides 0.9%, and H2O-sol. polysaccharides 0.8%. D-Glucose, D-galactose, D-mannose, L-fucose, L-arabinose, D-xylose, and D-galacturonic acid were detected as the component sugars. Antitumor active .**beta**.-D-**glucans**, inactive .**beta**.-D-**glucan**, .alpha.-D-**glucans** and heterogalactans were obtained by fractionation of the polysaccharides. By various chromatog. methods, gel chromatog., electrophoresis, and ultracentrifugation, 3 .**beta**.-D-**glucans** were obtained. Chem. analyses and 1H- and 13C-NMR showed that the 3 .**beta**.-D-**glucans** were composed of a linear .**beta**.-(1.fwdarw.3)-linked D-glucopyranosyl backbone having a single .**beta**.-(1.fwdarw.6)-glucopyranoside branch for every 3-5 .**beta**.-(1.fwdarw.3)-glucopyranoside linear linkages, with mol. wts. of 1.05 .times. 106, 3.12 .times. 105, and 2.43 .times. 103, resp. The first two .**beta**.-D-**glucans** markedly inhibited the growth of Sarcoma 180 in mice given at 1-5 mg/kg.

The third .**beta**.-D-**glucan** did not show any antitumor activity.

ST antitumor polysaccharide Ganoderma fruit body; heterogalactan antitumor Ganoderma fruit body; glucan antitumor Ganoderma fruit body

IT Polysaccharides, biological studies
RL: BIOL (Biological study)
(isolation from Ganoderma applanitum and neoplasm inhibiting activity and structure of)

IT Molecular structure, natural product
(of glucans of Ganoderma applanitum)

IT Ganoderma applanatum
(polysaccharides isolation from, neoplasm inhibiting activity and structure of)

IT Neoplasm inhibitors
(polysaccharides of Ganoderma applanitum)

IT **9041-22-9**
RL: BIOL (Biological study)
(isolation from Ganoderma applanitum and neoplasm inhibiting activity and structure of)

IT **9037-55-2D**, hetero- 9074-78-6 53238-80-5
RL: BIOL (Biological study)
(isolation from Ganoderma applanitum and neoplasm inhibiting activity of)

L126 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:404930 HCAPLUS
DN 95:4930
TI **Conformational** analysis of antigenic polysaccharides (.alpha.1 .fwdarw. 6)-D-**glucan** and (.**beta**.1 .fwdarw. 6)-D-galactan
AU Lipkind, G. M.; Kochetkov, N. K.
CS N. D. Zelinskii Inst. Org. Chem., Moscow, USSR
SO Bioorg. Khim. (**1981**), 7(5), 721-8
CODEN: BIKHD7
DT Journal
LA Russian
CC **15-2** (Immunochemistry)
Section cross-reference(s): 33
AB Theor. conformation anal. was carried out for (.alpha.1.fwdarw.6)-D-**glucan** and (.**beta**.1.fwdarw.6)-D-galactan. The optimal structures of the polymers and the conformations which allow these antigenic polysaccharides to interact with antibodies were detd.
ST glucan galactan conformation antigenicity
IT Chains, chemical
(conformation of, of galactan and glucan antigens, antibody interaction in relation to)

IT Antigens
RL: BIOL (Biological study)
(determinants, of galactan and glucan, conformation in relation to)

IT Antibodies
RL: BIOL (Biological study)
(galactan and glucan structure in relation to interaction with)

IT 9012-72-0 **9037-55-2**
RL: PRP (Properties)
(structure and conformation of, interaction with antibodies in relation to)

L126 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:58110 HCAPLUS
DN 94:58110
TI Antimacrophage agents decrease the **antitumor** effect of a water-soluble carboxymethylated (1 .fwdarw. 3)-.**beta**.-D-**glucan**
AU Sasaki, Takuma; Tanaka, Motohiro
CS Res. Inst., Natl. Cancer Cent., Tokyo, 104, Japan
SO Eur. J. Cancer (**1980**), 16(9), 1271-3

CODEN: EJCAAH; ISSN: 0014-2964
DT Journal
LA English
CC **1-5** (Pharmacodynamics)
AB Antimacrophage agents such as silica and **carrageenan** significantly decreased the antitumor activity of noncytotoxic carboxymethylglucan (I) [61163-25-5] in mice with transplanted sarcoma 180 ascites tumor. Poly-2-vinylpyridine N-oxide, a macrophage stabilizing agent, reversed the effects of the antimacrophage agents on the activity of I. In vitro, I had no direct cytotoxic effects; macrophages obtained from tumor-bearing control mice also did not alter tumor cell proliferation. However, macrophages obtained 10 days after the last I administration caused a 60% inhibition of tumor cell proliferation. Thus, in vivo and in vitro studies with macrophages indicate that the antitumor activity of I is immunol. nonspecific and is mediated by macrophages.
ST macrophage polysaccharide antitumor
IT Macrophage
(neoplasm inhibiting activity of polysaccharide mediation by)
IT 61163-25-5
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neoplasm inhibiting activity of, macrophages mediation of)

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L127 ANSWER 1 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **237069-85-1** REGISTRY
CN .iota.-Neocarradodecaose (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:161631

L127 ANSWER 2 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **237069-79-3** REGISTRY
CN .iota.-Neocarradecaose (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:161631

L127 ANSWER 3 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **237069-76-0** REGISTRY
CN .iota.-Neocarraoctaose (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:161631

L127 ANSWER 4 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **237069-74-8** REGISTRY
CN .iota.-Neocarrahexaose (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:161631

L127 ANSWER 5 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **237069-70-4** REGISTRY
CN .iota.-Neocarratetraose (9CI) (CA INDEX NAME)
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:161631

L127 ANSWER 6 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **39475-64-4** REGISTRY
CN D-Galactan, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN D-Galactan sulfate
CN DH 6322
CN Galactan sulfate
CN Polygalactose sulfate
DR 55787-14-9, 60001-17-4
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: ADISINSIGHT, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, MEDLINE, NAPRALERT, PHAR, TOXLIT, USPATFULL

CM 1

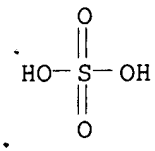
CRN 9037-55-2
CMF Unspecified

CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



50 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
50 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:55843

REFERENCE 2: 133:317030

REFERENCE 3: 133:147274

REFERENCE 4: 133:140242

REFERENCE 5: 132:317720

REFERENCE 6: 132:105537

REFERENCE 7: 131:161631

REFERENCE 8: 129:227868

REFERENCE 9: 128:225848

REFERENCE 10: 126:28866

L127 ANSWER 7 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **11016-36-7** REGISTRY
CN Porphyran (8CI, 9CI) (CA INDEX NAME)
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, MEDLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
44 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
44 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:55843

REFERENCE 2: 134:27460

REFERENCE 3: 133:134377

REFERENCE 4: 133:105237

REFERENCE 5: 132:92497

REFERENCE 6: 132:63286

REFERENCE 7: 132:30858

REFERENCE 8: 131:324052

REFERENCE 9: 131:161631

REFERENCE 10: 130:60714

L127 ANSWER 8 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9062-07-1** REGISTRY
CN .iota.-Carrageenan (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .beta.-Carrageenan 2,4'-bis(hydrogen sulfate)
CN .iota.-Carrageenin
CN Aubygel X 52
CN Carrageenan CSI 1
CN CSI 1
CN Deltagel 552
CN Eucheuma spinosum gum
CN Gelcarin GP 3367
CN Gelcarin ME 389
CN Gelcarin ME 621
CN Gelcarin SI
CN Genuvisco JJ
CN Genuvisco X 0908
CN Hygel SI 230
CN Pellugel ID
CN SeaSpen PF
CN Soageena MV 201
CN Soageena MV 220
CN Soageena MV 320
CN Soageena MV 330
CN Viscarin ME 389
CN Viscarin SD 309
DR 9079-01-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, IPA, NAPRALERT, NIOSHTIC, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
736 REFERENCES IN FILE CA (1967 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
738 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:344602

REFERENCE 2: 134:339857

REFERENCE 3: 134:271270

REFERENCE 4: 134:256725

REFERENCE 5: 134:227233

REFERENCE 6: 134:227226

REFERENCE 7: 134:227225

REFERENCE 8: 134:223285

REFERENCE 9: 134:192537

REFERENCE 10: 134:191956

L127 ANSWER 9 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9051-97-2** REGISTRY
CN .beta.-D-Glucan, (1.fwdarw.3)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (1,3)-.beta.-Glucan
CN (1.fwdarw.3)-.beta.-D-Glucan
CN Adjuvax
CN Drieline
CN GL 32
CN Glucan F
CN Guardoran
CN Highcareen GS
CN ImmuStim
CN Poly(1.fwdarw.3)-.beta.-D-glucan
CN Polysaccharide 13140
CN SSG
CN TAK
CN TAK (polysaccharide)
CN TAK-N
CN Uniglucan 51
CN VitaStim
DR 9050-90-2, 9052-00-0, 130809-04-0, 31667-87-5, 199665-06-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1014 REFERENCES IN FILE CA (1967 TO DATE)
119 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1015 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:349966

REFERENCE 2: 134:349702

REFERENCE 3: 134:348038

REFERENCE 4: 134:338155

REFERENCE 5: 134:330776

REFERENCE 6: 134:330763

REFERENCE 7: 134:261872

REFERENCE 8: 134:256583

REFERENCE 9: 134:251313

REFERENCE 10: 134:234206

L127 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9041-22-9** REGISTRY
CN .beta.-D-Glucan (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .beta.-Glucan
CN .beta.-Glucosylglucan

CN Biopoly P 3
CN Epiglucan
CN Fibosel
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CABA, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, IFICDB, IFIPAT, IFIUDB, IPA, NIOSHTIC, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1383 REFERENCES IN FILE CA (1967 TO DATE)
54 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1387 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:352534

REFERENCE 2: 134:339847

REFERENCE 3: 134:316161

REFERENCE 4: 134:310037

REFERENCE 5: 134:307135

REFERENCE 6: 134:285018

REFERENCE 7: 134:280084

REFERENCE 8: 134:265585

REFERENCE 9: 134:265579

REFERENCE 10: 134:265281

L127 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9037-55-2** REGISTRY
CN D-Galactan (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Galactan
AR 39300-87-3
DR 9046-30-4, 9065-98-9
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CHEMLIST, CIN, EMBASE, IFICDB, IFIPAT, IFIUDB, NAPRALERT, PIRA, PROMT, TOXLIT, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
473 REFERENCES IN FILE CA (1967 TO DATE)
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
475 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:349830

REFERENCE 2: 134:339847

REFERENCE 3: 134:251264

REFERENCE 4: 134:204806

REFERENCE 5: 134:192256

REFERENCE 6: 134:190425

REFERENCE 7: 134:177523

REFERENCE 8: 134:163832

REFERENCE 9: 134:159963

REFERENCE 10: 134:97632

L127 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9002-18-0** REGISTRY
CN Agar (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Agar-agar (8CI)
OTHER NAMES:
CN Agar Agar Flake
CN Agargel
CN Agaropectin, mixt. with agarose
CN Agarose, mixt. with agaropectin
CN Bacto-agar
CN Bengal gelatin
CN Bengal isinglass
CN Ceylon isinglass
CN Chinese isinglass
CN D 100
CN D 100 (polysaccharide)
CN Deltagar LTS
CN Difco Bacto agar
CN Digenea simplex mucilage
CN GAM medium
CN Gelose
CN Japan agar
CN Japan isinglass
CN Kantenmatsu
CN Layor Carang
CN Luxara 1253
CN Oxoid III
CN Oxoid L 11
CN Phytagar
CN S 100
CN S 100 (polysaccharide)
CN UP 37
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3642 REFERENCES IN FILE CA (1967 TO DATE)
76 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3651 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:357388

REFERENCE 2: 134:356923

REFERENCE 3: 134:354770

REFERENCE 4: 134:354244

REFERENCE 5: 134:352588

REFERENCE 6: 134:350195

REFERENCE 7: 134:339847

REFERENCE 8: 134:338289

REFERENCE 9: 134:337939

REFERENCE 10: 134:337791

L127 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2001 ACS
RN **9000-07-1** REGISTRY
CN Carrageenan (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .kappa..lambda.-Carrageenan
CN Aubygum x 2
CN Aubygum X 23
CN Carrageenan GH
CN Carrageenan gum
CN Carrageenan SWG-J
CN Carrageenin
CN Carragheen
CN Carragheenan
CN EC 4000
CN FK 6101
CN FK 6120
CN Gelcarin GP 37ANF
CN Gelcarin HWG
CN Gelloid J
CN Gelozone
CN Genugel LC 4
CN Genugel LC 5
CN Genugel MG 11
CN Genugel RLV
CN Genuvisco J
CN Gum carrageenan
CN Gum chon 2
CN Gum chond
CN Inagel E 150
CN LSS 1
CN ME 913
CN Newgelin LB 4
CN Norsk gelatan
CN Pellugel
CN Pencogel
CN Satiagel NP 5B
CN Sea-Pi Gum FA
CN Seagel GH
CN Seagel Pet
CN SeaKem carrageenin
CN Sherex IC 109
CN Soa Ace WX 138
CN Soageena MM 501
CN Soageena MW 351
CN Soageena WX 560
CN Takaragen L
CN TIC Pretested Colloid 775
CN TK 1
CN TK 1 (polysaccharide)
CN Viscarin IC 3820
CN Viscarin SD 389
CN Viscarin TP 389

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CN   X 5189
DR   8040-42-4, 9000-13-9, 9000-27-5, 78005-48-8
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration, Polyother, Polyother only
LC   STN Files:   AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT,
       APIPAT2, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS,
       CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE,
       HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
       NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            3467 REFERENCES IN FILE CA (1967 TO DATE)
             107 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            3475 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  134:357411

REFERENCE   2:  134:357388

REFERENCE   3:  134:357359

REFERENCE   4:  134:354003

REFERENCE   5:  134:352373

REFERENCE   6:  134:350284

REFERENCE   7:  134:344332

REFERENCE   8:  134:339857

REFERENCE   9:  134:339847

REFERENCE  10:  134:338705


=> fil medline
FILE 'MEDLINE' ENTERED AT 10:42:00 ON 13 JUN 2001

 FILE LAST UPDATED: 11 JUN 2001 (20010611/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains new records from the former NLM HEALTH STAR
 database.  These records have an Entry Date and Update Date of 20010223.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d all tot l158

L158 ANSWER 1 OF 9  MEDLINE
AN   1999218620     MEDLINE
```

DN 99218620 PubMed ID: 10200509
TI The role of phosphatidylserine in recognition of **apoptotic** cells by phagocytes.
CM Comment in: Cell Death Differ. 1998 Jul;5(7):549-50
AU Fadok V A; Bratton D L; Frasch S C; Warner M L; Henson P M
CS Department of Pediatrics, National Jewish Medical and Research Center, 1400 Jackson Street, Denver, Colorado 80206 USA.. fadokv@njc.org
SO CELL DEATH AND DIFFERENTIATION, **(1998 Jul)** 5 (7) 551-62. Ref: 128
Journal code: C7U; 9437445. ISSN: 1350-9047.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990607
Last Updated on STN: 20000303
Entered Medline: 19990527
AB Exposure of phosphatidylserine on the outer leaflet of the plasma membrane is a surface change common to many **apoptotic** cells. Normally restricted to the inner leaflet, phosphatidylserine appears as a result of decreased aminophospholipid translocase activity and activation of a calcium-dependent scramblase. Phosphatidylserine exposure has several potential biological consequences, one of which is recognition and removal of the **apoptotic** cell by phagocytes. It is still not clear which receptors mediate PS recognition on **apoptotic** cells; however, several interesting candidates have been proposed. These include the Class B scavenger and thrombospondin receptor CD36, an oxLDL receptor (CD68), CD14, annexins, beta2 glycoprotein I, gas-6 and a novel activity expressed on macrophages stimulated with digestible particles such as **beta -glucan.** Whether PS is the sole ligand recognized by phagocytes or whether it associated with other molecules to form a complex ligand remains to be determined.
CT Check Tags: Animal; Human
***Apoptosis**
*Phagocytes: PH, physiology
*Phosphatidylserines: PH, physiology
CN 0 (Phosphatidylserines)

L158 ANSWER 2 OF 9 MEDLINE
AN 1999081749 MEDLINE
DN 99081749 PubMed ID: 9864222
TI Modulation of endotoxin- and enterotoxin-induced cytokine release by in vivo treatment with beta-(1,6)-branched **beta**-(1,3)-**glucan.**
AU Soltys J; Quinn M T
CS Department of Veterinary Molecular Biology, Montana State University, Bozeman 59717, USA.
NC S10 RR11877 (NCRR)
SO INFECTION AND IMMUNITY, **(1999 Jan)** 67 (1) 244-52.
Journal code: GO7; 0246127. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990209
Last Updated on STN: 19990209
Entered Medline: 19990128
AB Leukocytes activated by endotoxin or enterotoxins release proinflammatory cytokines, thereby contributing to the cascade of events leading to septic shock. In the present studies, we analyzed the effects of in vivo administration of a soluble immunomodulator, beta-(1,6)-branched **beta**-(1,3)-**glucan** (soluble **beta-glucan**

), on toxin-stimulated cytokine production in monocytes and lymphocytes isolated from treated mice. In vitro stimulation of lymphocytes isolated from soluble **beta-glucan**-treated mice with lipopolysaccharide (LPS) resulted in enhanced production of interleukin-6 (IL-6) and suppressed production of tumor necrosis factor alpha (TNF-alpha), while stimulation of these cells with staphylococcal enterotoxin B (SEB) or toxic shock syndrome toxin 1 (TSST-1) resulted in enhanced production of gamma interferon (IFN-gamma) and suppressed production of IL-2 and TNF-alpha compared to that in cells isolated from untreated mice. In vitro stimulation of monocytes isolated from soluble **beta-glucan**-treated mice with LPS also resulted in suppressed TNF-alpha production, while stimulation of these cells with SEB or TSST-1 resulted in suppressed IL-6 and TNF-alpha production compared to that in cells isolated from untreated mice. Thus, the overall cytokine pattern of leukocytes from soluble **beta-glucan**-treated mice reflects suppressed production of proinflammatory cytokines, especially TNF-alpha. Taken together, our results suggest that treatment with soluble **beta-glucan** can modulate the induction cytokines during sepsis, resulting in an overall decrease in host mortality.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Adjuvants, Immunologic: AD, administration & dosage
Apoptosis: DE, drug effects
Apoptosis: IM, immunology
*Cytokines: ME, metabolism
*Enterotoxins: PD, pharmacology
***Glucans: AD, administration & dosage**
Injections, Intramuscular
***Lipopolysaccharides: PD, pharmacology**
Lymphocytes: IM, immunology
Lymphocytes: ME, metabolism
Mice
Mice, Inbred BALB C
Monocytes: IM, immunology
Monocytes: ME, metabolism
Staphylococcus aureus: IM, immunology
Superantigens: PD, pharmacology

RN **37361-00-5 (beta-glucan (1-6))**; 39424-53-8 (enterotoxin B, staphylococcal); **9051-97-2 (beta-1,3-glucan)**

CN 0 (Adjuvants, Immunologic); 0 (Cytokines); 0 (Enterotoxins); **0 (Glucans)**; 0 (Lipopolysaccharides); 0 (Superantigens); 0 (enterotoxin F, Staphylococcal)

L158 ANSWER 3 OF 9 MEDLINE
AN 1999049859 MEDLINE
DN 99049859 PubMed ID: 9834113
TI CD36 is required for phagocytosis of **apoptotic** cells by human macrophages that use either a phosphatidylserine receptor or the vitronectin receptor (alpha v beta 3).
AU Fadok V A; Warner M L; Bratton D L; Henson P M
CS Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO 80206, USA.. fadokv@njc.org
NC R01GM48211 (NIGMS)
SO JOURNAL OF IMMUNOLOGY, **(1998 Dec 1)** 161 (11) 6250-7.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221
AB In vivo, **apoptotic** cells are efficiently removed by professional or nonprofessional phagocytes, a process thought to be essential for

tissue remodeling and resolution of inflammation. Macrophages recognize **apoptotic** cells by several mechanisms, including recognition of exposed phosphatidylserine (PS); however, PS recognition on **apoptotic** cells has not been identified as a feature of human macrophages. The purpose of this study was to determine whether human monocyte-derived macrophages could be stimulated to recognize PS, defined as inhibition of phagocytosis by PS-containing liposomes. We also assessed the potential roles for scavenger receptors, CD14, and lectins. Uptake of **apoptotic** neutrophils into unstimulated macrophages was blocked about 50% by Arg-Gly-Asp-Ser and anti-alpha(v), and up to 20% by oxidized low density lipoprotein and N-acetylglucosamine, implying a major role for integrin and minor roles for scavenger and lectin receptors. Uptake into macrophages stimulated with **beta**-1,3-**glucan** was blocked 50% by PS liposomes and 40% by oxidized low density lipoprotein, suggesting that the macrophages had switched from using integrin to recognition of PS. MEM-18 and 61D3 (anti-CD14 mAbs) were poor inhibitors of **apoptotic** neutrophil uptake, but good inhibitors of **apoptotic** lymphocyte uptake. The switch to PS recognition was accompanied by down-regulation of alpha(v)beta3 expression and function. Anti-CD36 blocked uptake into unstimulated or stimulated macrophages, suggesting CD36 involvement not only with the alpha(v)beta3 integrin mechanism (as previously reported) but also with PS recognition. A maximum of 70% inhibition was achieved by combining anti-CD36 with either anti-a(v) or PS liposomes.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Antigens, CD14: PH, physiology
Antigens, CD36: ME, metabolism
*Antigens, CD36: PH, physiology
***Apoptosis: IM, immunology**
Bacterial Proteins: ME, metabolism
Macrophages: IM, immunology
*Macrophages: ME, metabolism
*Phagocytosis: IM, immunology
*Phosphatidylserines: ME, metabolism
*Receptors, Cell Surface: PH, physiology
Receptors, Mitogen: PH, physiology
*Receptors, Vitronectin: PH, physiology

CN 0 (Antigens, CD14); 0 (Antigens, CD36); 0 (Bacterial Proteins); 0 (Phosphatidylserines); 0 (Receptors, Cell Surface); 0 (Receptors, Mitogen); 0 (Receptors, Vitronectin); 0 (msrA protein)

L158 ANSWER 4 OF 9 MEDLINE
AN 1998380290 MEDLINE
DN 98380290 PubMed ID: 9712725
TI Ligand binding to the (1 --> 3)-**beta**-D-**glucan** receptor stimulates NFkappaB activation, but not **apoptosis** in U937 cells.
AU Battle J; Ha T; Li C; Della Beffa V; Rice P; Kalbfleisch J; Browder W; Williams D
CS James H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee, 37614-0575, USA.
NC GM53522 (NIGMS)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1998 Aug 19)** 249 (2) 499-504.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980911
AB Recent data suggest that sepsis stimulates macrophage **apoptosis** (Ao) with subsequent induction of macrophage dysfunction. Nuclear factor-kappaB (NFkappaB) activation has been linked to Ao in either a pro-

or antiapoptotic role. **Glucans** are biological response modifiers which exert antisepsis activity. This investigation examined the effect of (1-3)-**beta**-D-**glucan** receptor binding by a high affinity ligand on Ao and NFkappaB activation in U937 cells in the presence or absence of LPS. A high affinity **glucan** ligand (IC50 = 23 nM) activated NFkappaB, but did not induce Ao or significantly alter LPS induced U937 Ao. These data indicate that: i) modulation of the macrophage (1-3)-**beta**-D-**glucan** receptor stimulates NFkappaB; ii) does not induce Ao or significantly diminish LPS induced Ao and iii) activation of the U937 FAS receptor does not alter the relative Ao responses in **glucan** and LPS treated cells.
Copyright 1998 Academic Press.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Antibodies: ME, metabolism
Antibodies: PD, pharmacology
***Apoptosis**
Cell Line
Escherichia coli
***Glucans: ME, metabolism**
Ligands
Lipopolysaccharides: PD, pharmacology
*Macrophages: ME, metabolism
Membrane Glycoproteins: IM, immunology
Membrane Glycoproteins: ME, metabolism
*NF-kappa B: ME, metabolism
*Receptors, Immunologic: ME, metabolism
RN **39464-87-4 (scleroglucan); 9051-97-2 (beta-1,3-glucan)**
CN 0 (Antibodies); 0 (FasL protein); **0 (Glucans)**; 0 (Ligands); 0 (Lipopolysaccharides); 0 (Membrane Glycoproteins); 0 (NF-kappa B); 0 (Receptors, Immunologic); 0 (**beta-glucan** receptor)

L158 ANSWER 5 OF 9 MEDLINE
AN 1998287220 MEDLINE
DN 98287220 PubMed ID: 9625538
TI Selective tumoricidal effect of soluble **proteoglucan** extracted from the basidiomycete, Agaricus blazei Murill, mediated via natural killer cell activation and **apoptosis**.
AU Fujimiya Y; Suzuki Y; Oshiman K; Kobori H; Moriguchi K; Nakashima H; Matumoto Y; Takahara S; Ebina T; Katakura R
CS Division of Immunology, Miyagi Cancer Center Research Institute, Natori, Japan.
SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, **(1998 May)** 46 (3) 147-59.
Journal code: CN3; 8605732. ISSN: 0340-7004.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
ED Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709
AB We have isolated a novel type of natural tumoricidal product from the basidiomycete strain, Agaricus blazei Murill. Using the double-grafted tumor system in Balb/c mice, treatment of the primary tumor with an acid-treated fraction (ATF) obtained from the fruit bodies resulted in infiltration of the distant tumor by natural killer (NK) cells with marked tumoricidal activity. As shown by electrophoresis and DNA fragmentation assay, the ATF also directly inhibited tumor cell growth in vitro by inducing **apoptotic** processing; this **apoptotic** effect was also demonstrated by increased expression of the Apo2.7 antigen on the mitochondrial membranes of tumor cells, as shown by flow-cytometric analysis. The ATF had no effect on normal mouse splenic or interleukin-2-treated splenic mononuclear cells, indicating that it is selectively cytotoxic for the tumor cells. Cell-cycle analysis demonstrated that ATF induced the loss of S phase in MethA tumor cells, but did not affect normal splenic mononuclear cells, which were mainly in

the G0G1 phase. Various chromatofocussing purification steps and NMR analysis showed the tumoricidal activity to be chiefly present in fractions containing (1-->4)-alpha-D-**glucan** and (1-->6)-**beta**-D-**glucan**, present in a ratio of approximately 1:2 in the ATF (molecular mass 170 kDa), while the final purified fraction, HM3-G (molecular mass 380 kDa), with the highest tumoricidal activity, consisted of more than 90% glucose, the main component being (1-->4)-alpha-D-**glucan** with (1-->6)-beta branching, in the ratio of approximately 4:1.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
*Agaricus: CH, chemistry
*Agaricus: IM, immunology
Antigens, Surface: GE, genetics
***Apoptosis: IM, immunology**
Carcinogens: PD, pharmacology
Cell Cycle: DE, drug effects
Chromatography
*Cytotoxicity, Immunologic: DE, drug effects
*Cytotoxicity, Immunologic: IM, immunology
DNA Fragmentation: DE, drug effects
Fungal Proteins: CH, chemistry
*Fungal Proteins: IM, immunology
*Fungal Proteins: PD, pharmacology
Immunophenotyping
*Killer Cells, Natural: IM, immunology
Leukocyte Count: DE, drug effects
Leukocytes, Mononuclear: CY, cytology
Leukocytes, Mononuclear: DE, drug effects
Leukocytes, Mononuclear: IM, immunology
Lymphocyte Transformation: PH, physiology
Magnetic Resonance Spectroscopy
Membrane Proteins: AN, analysis
Methylcholanthrene: PD, pharmacology
Mice
Mice, Inbred BALB C
Mitochondria: CH, chemistry
Neoplasm Transplantation
Neoplasms, Experimental: IM, immunology
Phenotype
Proteoglycans: CH, chemistry
***Proteoglycans: IM, immunology**
***Proteoglycans: PD, pharmacology**
Spleen: CY, cytology
Spleen: IM, immunology
Transplants
Tumor Cells, Cultured: CH, chemistry
Tumor Cells, Cultured: DE, drug effects

RN 56-49-5 (Methylcholanthrene)
CN 0 (Antigens, Surface); 0 (Carcinogens); 0 (Fungal Proteins); 0 (Membrane Proteins); 0 (Proteoglycans)

L158 ANSWER 6 OF 9 MEDLINE
AN 1998059976 MEDLINE
DN 98059976 PubMed ID: 9397587
TI Cytotoxic effect against HeLa cells of polysaccharides from the lichen Ramalina celastri.
AU Leao A M; Buchi D F; Iacomini M; Gorin P A; Oliveira M B
CS Department of Animal Morphology and Physiology, Federal Rural University of Pernambuco, Recife, PE, Brazil.
SO JOURNAL OF SUBMICROSCOPIC CYTOLOGY AND PATHOLOGY, **(1997 Oct)** 29 (4) 503-9.
Journal code: CMS; 8804312. ISSN: 1122-9497.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199801
ED Entered STN: 19980129
Last Updated on STN: 20000303
Entered Medline: 19980114
AB The most active polysaccharides which show anti-tumoral activity are (1-->3)-**beta**-D-**glucans**, branched or not at O-6. Since these structures are sometimes poorly soluble in aqueous media, alpha-D-**glucans** and their chemical derivatives, which are more soluble, were also studied. The present object is to observe morphological alterations in HeLa cells caused by two different polysaccharides obtained from the lichen Ramalina celastri, which are (1-->3),(1-->4)-linked alpha-D-**glucan** and its sulphated derivative. The cells were incubated in Eagle's medium in the absence or presence of each polysaccharide and routinely processed and analysed by light and electron microscopy. Even though the alpha-D-**glucan** altered the cellular volume, cytoplasmic densities, and mitosis, the resulting monolayer was similar to the control. TEM analysis showed cytoplasmic blebbing and the presence of an amorphous electron-dense material free in the cytoplasm and interior membranes. The enhanced injury caused by the sulphated derivative was apparent, altering cell adhesion and causing cell aggregation. Nuclear modifications such as fragmentation and condensation of chromatin under the nuclear envelope, which showed to be convoluted, suggested the occurrence of cell death by **apoptosis**.
CT Check Tags: Human
*Hela Cells: DE, drug effects
*Hela Cells: PA, pathology
Hela Cells: UL, ultrastructure
*Lichens: ME, metabolism
Microscopy, Electron
***Polysaccharides: TO, toxicity**
CN 0 (Polysaccharides)

L158 ANSWER 7 OF 9 MEDLINE
AN 96268732 MEDLINE
DN 96268732 PubMed ID: 8687449
TI Macrophage cytotoxicity against murine meth A sarcoma involves nitric oxide-mediated **apoptosis**.
AU Sveinbjornsson B; Olsen R; Seternes O M; Seljelid R
CS Institute of Medical Biology, University of Tromso, Norway.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1996 Jun 25)** 223 (3) 643-9.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960828
Last Updated on STN: 19970203
Entered Medline: 19960816
AB We have studied the cytotoxic effect of stimulated macrophages on Meth A tumor cells in vitro. When stimulated with interferon-gamma and soluble **beta**-1,3-D-**glucan**, macrophages exerted cytotoxicity towards syngeneic Meth A tumor cells. This cytotoxicity was associated with a high level of nitric oxide production. Both cell death and nitric oxide production were significantly inhibited by the addition of aminoguanidine, a specific inhibitor of inducible nitric oxide synthase (iNOS), to the culture medium. The cytotoxic effect was accompanied by internucleosomal cleavage of DNA as shown by electrophoresis and DNA fragmentation assay.
CT Check Tags: Animal; Female
***Apoptosis**
Cells, Cultured
Coculture
***Glucans: PD, pharmacology**
Guanidines: PD, pharmacology

*Interferon Inducers: PD, pharmacology
*Interferon-gamma, Recombinant: PD, pharmacology
*Macrophage Activation
Macrophage Activation: DE, drug effects
Macrophages, Peritoneal: DE, drug effects
*Macrophages, Peritoneal: IM, immunology
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Microscopy, Electron
Microscopy, Electron, Scanning
*Nitric Oxide: PH, physiology
Nitrites: ME, metabolism
*Nitroprusside: PD, pharmacology
*Sarcoma, Experimental: IM, immunology
Sarcoma, Experimental: PA, pathology
Sarcoma, Experimental: UL, ultrastructure
Tumor Cells, Cultured
RN 10102-43-9 (Nitric Oxide); 15078-28-1 (Nitroprusside); 79-17-4 (pimagedine); **9051-97-2 (beta-1,3-glucan)**
CN **0 (Glucans)**; 0 (Guanidines); 0 (Interferon Inducers); 0 (Interferon-gamma, Recombinant); 0 (Nitrites)

L158 ANSWER 8 OF 9 MEDLINE
AN 96094479 MEDLINE
DN 96094479 PubMed ID: 7499871
TI Autocrine/paracrine involvement of platelet-activating factor and transforming growth factor-beta in the induction of phosphatidylserine recognition by murine macrophages.
AU Rose D M; Fadok V A; Riches D W; Clay K L; Henson P M
CS Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206, USA.
NC AI09176 (NIAID)
GM48211 (NIGMS)
SO JOURNAL OF IMMUNOLOGY, **(1995 Dec 15)** 155 (12) 5819-25.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960118
AB The specific recognition of phosphatidylserine (PS) by macrophages is believed to be one means by which effete and **apoptotic** cells expressing PS on their outer membrane leaflet are targeted for phagocytosis. The aim of this study was to better understand the autocrine/paracrine factors involved in **beta-glucan** induction of PS recognition by macrophages. We provide evidence that both platelet-activating factor (PAF) and TGF-beta are involved in **beta -glucan** induction of PS recognition. This is based on the observations that the PAF receptor antagonist WEB 2086 and Ab against TGF-beta each could partially inhibit **beta-glucan** -induced PS recognition when used alone and could completely inhibit induction when used in combination. PAF, like TGF-beta, was found to prime macrophages for PS recognition, which could then be triggered by costimulation with a nonspecific phagocytic stimulus, latex particles. We also provide evidence that the priming by PAF and that by TGF-beta can occur independently of each other. This is based on the observations that 1) PAF priming was not blocked by anti-TGF-beta Ab, nor was TGF-beta priming prevented by WEB 2086; and 2) PAF did not increase the steady state level of TGF-beta mRNA, and TGF-beta did not induce PAF synthesis in these cells.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: IM, immunology

Bone Marrow: CY, cytology
Cells, Cultured
Glucans: PD, pharmacology
Macrophage Activation: DE, drug effects
Macrophages: DE, drug effects
*Macrophages: ME, metabolism
Mice
Mice, Inbred C3H
*Phosphatidylserines: ME, metabolism
*Platelet Activating Factor: PH, physiology
Platelet Membrane Glycoproteins: AI, antagonists & inhibitors
Transforming Growth Factor beta: IM, immunology
*Transforming Growth Factor beta: PH, physiology
CN 0 (Antibodies, Monoclonal); **0 (Glucans)**; 0 (Phosphatidylserines); 0 (Platelet Activating Factor); 0 (Platelet Membrane Glycoproteins); 0 (Transforming Growth Factor beta); 0 (platelet activating factor receptor)

L158 ANSWER 9 OF 9 MEDLINE
AN 94014371 MEDLINE
DN 94014371 PubMed ID: 8409401
TI Particle digestibility is required for induction of the phosphatidylserine recognition mechanism used by murine macrophages to phagocytose **apoptotic** cells.
AU Fadok V A; Laszlo D J; Noble P W; Weinstein L; Riches D W; Henson P M
CS Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.
NC CA50107 (NCI)
GM48211 (NIGMS)
HL27353 (NHLBI)
+
SO JOURNAL OF IMMUNOLOGY, **(1993 Oct 15)** 151 (8) 4274-85.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931109
AB One of the characteristic features of programmed cell death in vivo is the rapid recognition and removal of **apoptotic** cells by macrophages. Although there are several potential mechanisms by which the macrophage can identify a cell as **apoptotic**, it has been shown recently that murine-elicited macrophages stereospecifically recognize phosphatidylserine (PS) exposed on the surface of **apoptotic** cells. The particulate stimulus, **beta**-1, 3-**glucan**, stimulates bone marrow-derived macrophages to express several characteristics of inflammatory macrophages, and induced these cells to recognize PS on **apoptotic** cells; this activity was correlated with the ability to form rosettes with PS-expressing RBC. Induction of PS recognition in bone marrow-derived macrophages was associated with digestibility of the stimulus, because L, but not D amino acid particles or latex, were able to stimulate macrophage recognition of PS. The requirement for digestibility could be bypassed by the addition of exogenous TGF-beta, which induced macrophage recognition of PS after stimulation with either latex or D amino acid particles. That endogenously produced TGF-beta played a role in the **glucan**-stimulated response was indicated by the ability of anti-TGF-beta antibodies to inhibit digestible particle-induced recognition of PS. The induction of the PS recognition mechanism correlated well with the expression of other markers for the inflammatory phenotype. These studies indicate that the PS receptor may be a marker for the inflammatory phenotype, which appears to be induced by the phagocytosis of particulate digestible stimuli. Endogenously produced TGF-beta is suggested to play an autocrine or

paracrine priming role in the induction of the PS receptor.
CT Check Tags: Animal; Female; Male; Support, U.S. Gov't, P.H.S.
***Apoptosis**
Cells, Cultured
Diamide: PD, pharmacology
Glucans: PD, pharmacology
*Macrophages: PH, physiology
Mice
Mice, Inbred C3H
Mice, Inbred C57BL
Mice, Inbred DBA
*Phagocytosis
Phagocytosis: DE, drug effects
*Phosphatidylserines: ME, metabolism
Rosette Formation
Transforming Growth Factor beta: PD, pharmacology
RN 10465-78-8 (Diamide); **9051-97-2 (beta-1,3-glucan)**
CN **0 (Glucans)**; 0 (Phosphatidylserines); 0 (Transforming Growth Factor beta)

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FILE LAST UPDATED: 12 Jun 2001 (20010612/ED)

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=> d all tot

L162 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:456066 HCAPLUS
DN 125:96228
TI Keratan sulfate oligosaccharide fraction and drug containing the same
IN Maruyama, Hiroshi; Morikawa, Kiyoshi; Tawada, Akira; Miyauchi, Satoshi; Yoshida, Keiichi; Asari, Akira
PA Seikagaku Corporation, Japan
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07H011-00
ICS A61K031-70
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616973	A1	19960606	WO 1995-JP2386	19951122
	W: AU, CA, CN, HU, JP, KR, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2206611	AA	19960606	CA 1995-2206611	19951122
	AU 9539356	A1	19960619	AU 1995-39356	19951122
	AU 704429	B2	19990422		
	EP 795560	A1	19970917	EP 1995-937170	19951122 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1174557	A	19980225	CN 1995-197492	19951122
	HU 77134	A2	19980302	HU 1997-1820	19951122
	US 5939403	A	19990817	US 1997-849925	19970602
	US 6159954	A	20001212	US 1999-317380	19990524
PRAI	JP 1994-298298	A	19941201		
	WO 1995-JP2386	W	19951122		

AB This invention relates to a keratan sulfate oligosaccharide comprising a di- to penta-saccharide which has a sulfated N-aetylglucosamine at the reducing end and wherein at least two hydroxyl groups per mol. have been sulfated, preferably one contg. a disaccharide of the formula Aal(6S)-GlcNAc(6S) (wherein Gal, GlcN, Ac and 6S represent, resp., galactose, glucosamine, acetyl and 6-O-sulfate) as the constituent; and antiphlogistic agent, antiallergic agent, immunoregulator, cell differentiation inducer and apoptosis inducer each contg. the above oligosaccharide and/or a pharmaceutically acceptable salt thereof as the active ingredient. As an example, an eye lotion was formulated contg. the keratan sulfate oligosaccharide Gal(6S).beta.1-4GlcNAc(6S).beta.1-3Gal(6S).beta.1-4GlcNAc(6S) [wherein Gal, GlcN, Ac and 6S are same as above] 10 and Na hyaluronate 2 mg/mL in pH 6.8-7.6 phosphate buffer. Keratan sulfate oligosaccharides were obtained by enzymic hydrolysis of keratan sulfate prepd. from shark soft bone.

ST therapeutic keratan sulfate oligosaccharide

IT Inflammation inhibitors
(Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Allergy inhibitors
Immunomodulators
Oligosaccharides
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Animal cell
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(differentiation inducer; Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Apoptosis
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inducer; Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Bone
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(shark soft; therapeutic keratan sulfate oligosaccharide fraction from)

IT Shark
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(soft bone; therapeutic keratan sulfate oligosaccharide fraction from)

IT Pharmaceutical dosage forms
(injections, Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Pharmaceutical dosage forms
(liposomes, Keratan sulfate oligosaccharide fraction and drug contg. the same)

IT Pharmaceutical dosage forms

(ointments, Keratan sulfate oligosaccharide fraction and drug contg. the same)
IT Pharmaceutical dosage forms
(solns., ophthalmic, Keratan sulfate oligosaccharide fraction and drug contg. the same)
IT 144095-99-8P 179074-66-9P 179074-67-0P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Keratan sulfate oligosaccharides contg.; Keratan sulfate oligosaccharide fraction and drug contg. the same)
IT 9056-36-4P, Keratan sulfate
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligosaccharide; Keratan sulfate oligosaccharide fraction and drug contg. the same)

L162 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:541403 HCAPLUS
DN 122:283855
TI Regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands
IN Crabtree, Gerald R.; Schreiber, Stuart L.; Spencer, David M.; Wandless, Thomas J.; Belshaw, Peter
PA Board of Trustees of the Leland Stanford Junior University, USA; President and Fellows of Harvard College
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-00
ICS C12N015-00; C07H015-12; C07K015-00; A61K031-70
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 13, 64
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9502684	A1	19950126	WO 1994-US8008	19940718	<--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	WO 9418317	A1	19940818	WO 1994-US1617	19940214	
	W: AT, AU, BB, BG, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, SK					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9473363	A1	19950213	AU 1994-73363	19940718	
	AU 696991	B2	19980924			
	CN 1130401	A	19960904	CN 1994-193251	19940718	
	JP 09503645	T2	19970415	JP 1994-504752	19940718	
	EP 776359	A1	19970604	EP 1994-923515	19940718	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	FI 9600165	A	19960126	FI 1996-165	19960115	
	US 6063625	A	20000516	US 1998-156855	19980916	
	US 6140120	A	20001031	US 1998-158010	19980916	
PRAI	US 1993-93499	A	19930716			
	US 1994-179143	A	19940107			
	WO 1994-US1617	A	19940214			
	US 1993-17931	A	19930212			
	US 1993-92977	A	19930716			
	US 1994-179748	A	19940107			
	US 1994-196043	B1	19940211			
	WO 1994-US8008	W	19940718			

AB A general procedure is described for the regulated (inducible) dimerization or oligomerization of intracellular proteins and methods and

materials are presented for using that procedure to regulatably initiate cell-specific apoptosis (programmed cell death) in genetically engineered cells. The procedure involves chimeric (or fused) proteins, DNA constructs encoding them, and ligand mols. capable of oligomerizing the chimeric proteins. The chimeric proteins contain at least one ligand-binding (or receptor) domain fused to an action domain capable of initiating apoptosis within a cell, and may also contain addnl. domains for (1) the regulatable or constitutive expression of desired genes and (2) intracellular targeting. The chimeric proteins are capable of binding to an FK506-type ligand, a cyclosporin A-type ligand, tetracycline, or a steroid ligand. One such chimeric protein is myristoylated CD3/FKBP12 (MZF3E) receptor consisting of (1) a c-src fragment sufficient for myristoylation, (2) the cytoplasmic tail of .zeta. (a component of the B cell receptor), (3) 3 consecutive domains of the FKBP12 immunophilin, and (4) a flu epitope tag; oligomerization/apoptosis is induced by a dimeric deriv. of FK506. Syntheses are reported for the prepn. of dimeric and "bumped" (contg. steric bulky groups) derivs. of FK506 and cyclosporin A. The overall procedures allows ligand-mediated oligomerization for regulated gene therapy.

ST apoptosis programmed chimeric protein genetic engineering; FK506 binding chimeric protein apoptosis; cyclosporin binding chimeric protein apoptosis; FKBP12 chimeric protein programmed apoptosis; cyclophilin chimeric protein programmed apoptosis; Fas antigen chimeric protein programmed apoptosis

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(apoptosis-inducing, fusion products with ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products with apoptosis-inducing protein domains; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Apoptosis
(programmed; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Genetic engineering
Immunosuppressants
Pharmaceuticals
Transformation, genetic
(regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Virus, animal
(vector; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Antigen receptors
Receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BCR (B-cell antigen receptors), .zeta. chain cytoplasmic tail, fusion products with ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD3, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FKBP-12 (FK 506-binding protein, 12,000-mol.-wt.), fusion products with apoptosis-inducing protein domains; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Fas, fusion products with ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HNF-1 (hepatocyte nuclear factor 1), fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility antigen complex), class II, I-E chain signal peptide, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NLS (nuclear location signal sequence)-contg., fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Vmw65 (virion-assocd. stimulatory protein, 65,000-mol.-wt.), fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Virus, animal
(adeno-, vector; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Virus, animal
(adeno-assocd., vector; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclophilins, fusion products with apoptosis-inducing protein domains; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products, regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BPN

(Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene GAL4, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene c-src, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Therapeutics
(geno-, regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immunophilins, fusion products with apoptosis-inducing protein domains; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Lymphokine and cytokine receptors
Receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 2, Tac chain, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Virus, animal
(retro-, vector; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(signal, fusion products with apoptosis-inducing protein domains and ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT Lymphokine and cytokine receptors
Receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tumor necrosis factor-.alpha., fusion products with ligand-binding receptors; regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

IT 161140-27-8P 161140-28-9P 161140-29-0P 161140-30-3P 161140-31-4P 161140-32-5P 162926-19-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FK506-type and cyclosporin-type ligands for regulated apoptosis by chimeric proteins)

IT 100-46-9, Benzylamine, reactions 124-09-4, 1,6-Hexanediamine, reactions 373-44-4, 1,8-Octanediamine 539-48-0, p-Xylylenediamine 646-25-3, Decamethylenediamine 4097-89-6 38721-52-7 51857-17-1 89270-28-0 133941-75-0 138957-22-9 138957-23-0 161140-22-3
RL: RCT (Reactant)
(FK506-type and cyclosporin-type ligands for regulated apoptosis by chimeric proteins)

IT 133523-46-3P 152406-15-0P 152406-19-4P 152406-20-7P 154074-71-2P 155684-96-1P 161140-18-7P 161140-19-8P 161140-20-1P 161140-21-2P 161140-23-4P 161140-24-5P 161247-38-7P 162926-14-9P 162926-15-0P 162926-16-1P 162926-17-2P 162926-18-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(FK506-type and cyclosporin-type ligands for regulated apoptosis by chimeric proteins)

IT 111710-64-6P 111722-74-8P 134166-82-8P 134166-84-0P 161140-25-6P
161140-26-7P 162926-20-7P 162926-21-8P 162926-22-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(FK506-type and cyclosporin-type ligands for regulated apoptosis by chimeric proteins)

IT 60-54-8P, Tetracycline 53123-88-9P, Rapamycin 59865-13-3DP, Cyclosporin A, derivs. 104987-11-3DP, FK506, derivs. 104987-12-4P, FK520
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(regulated apoptosis by chimeric proteins binding to FK506-type and cyclosporin-type ligands)

L162 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:377088 HCAPLUS
DN 122:153359
TI Regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription
IN Crabtree, Gerald R.; Schreiber, Stuart L.; Spencer, David M.; Wandless, Thomas J.; Belshaw, Peter
PA Leland Stanford Junior University, USA; Harvard College
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-00
ICS C12N005-00; C12N005-06; C12N015-11; C12P021-06; C12P021-00
CC 3-1 (Biochemical Genetics)
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9418317	A1	19940818	WO 1994-US1617	19940214	
	W: AT, AU, BB, BG, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, SK					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CA 2155728	AA	19940818	CA 1994-2155728	19940214	
	AU 9462403	A1	19940829	AU 1994-62403	19940214	
	AU 690898	B2	19980507			
	CN 1119876	A	19960403	CN 1994-191558	19940214	
	HU 73101	A2	19960628	HU 1995-2370	19940214	
	EP 804561	A1	19971105	EP 1994-909629	19940214	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
	CA 2167282	AA	19950126	CA 1994-2167282	19940718	
	WO 9502684	A1	19950126	WO 1994-US8008	19940718	<--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9473363	A1	19950213	AU 1994-73363	19940718	
	AU 696991	B2	19980924			
	HU 73100	A2	19960628	HU 1996-83	19940718	
	JP 09503645	T2	19970415	JP 1994-504752	19940718	
	US 5871753	A	19990216	US 1995-473985	19950607	
	FI 9503812	A	19950811	FI 1995-3812	19950811	
	FI 9600165	A	19960126	FI 1996-165	19960115	
	AU 9878807	A1	19981008	AU 1998-78807	19980806	
	US 6063625	A	20000516	US 1998-156855	19980916	
	US 6140120	A	20001031	US 1998-158010	19980916	
PRAI	US 1993-17931	A	19930212			
	US 1993-92977	A	19930716			

US 1994-179748 A 19940107
US 1993-93499 A 19930716
US 1994-179143 A 19940107
US 1994-196043 B1 19940211
WO 1994-US1617 W 19940214
WO 1994-US8008 W 19940718

AB A general procedure for regulating (inducing) dimerization or oligomerization of chimeric proteins is presented. The chimeric proteins contain a receptor domain and another protein domain capable of initiating a biol. process. The chimeric proteins can be induced to assoc. by treating the cells or organisms that harbor them with cell-permeable, synthetic ligands. The dimers/oligomers bind to a transcription control element and stimulate transcription of the gene to which it is assocd. The syntheses of FK-506 dimers are presented. Such dimers were used to induce: (1) the intracellular aggregation of the cytoplasmic tail of the zeta chain of the T cell receptor (TCR)-CD3 complex thereby leading to signaling and transcription of a reporter gene, (2) the homodimerization of the cytoplasmic tail of the Fas receptor thereby leading to cell-specific apoptosis (programmed cell death) and (3) the heterodimerization of a DNA-binding domain (Gal4) and a transcription-activation domain (VP16) thereby leading to direct transcription of a reporter gene.

ST gene transcription regulation ligand dimer; receptor protein chimeric oligomerization transcription

IT Nucleic acids
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antisense; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Ribonucleic acid formation factors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusion protein with receptor; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(intracellular targeting; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Animal cell
(mammalian; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Animal
Apoptosis
Cell
Insect
Mammal
Mouse
Plant
Rodent
Transcription, genetic
Worm
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Ribozymes
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Ligands
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Steroids, reactions
RL: RCT (Reactant)
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(surface membrane or secreted or cytoplasmic; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transcription control element; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(CD3, .zeta. subunit, fusion protein with receptor; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNA-binding, fusion protein with receptor; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Fas, fusion products with immunophilins; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Virus, animal
(adeno-, vector; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Virus, animal
(adeno-assocd., vector; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chimeric, regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cyclophilins, fusion products with Fas antigens; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Ribonucleic acid formation factors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene GAL4, fusion products with immunophilins; regulated transcription

of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Proteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(immunophilins, fusion products with CD3; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT Virus, animal
(retro-, vector; regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT 161140-21-2P 161140-27-8P 161140-28-9P 161140-29-0P 161140-30-3P
161140-31-4P 161140-32-5P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of immunophilin dimers for regulation of transcription of target genes)

IT 100-46-9, Benzylamine, reactions 539-48-0, p-Xylylenediamine
74124-79-1, N,N'-Disuccinimidyl carbonate 133523-46-3 133941-75-0
138957-23-0 161140-22-3
RL: RCT (Reactant)
(prepn. of immunophilin dimers for regulation of transcription of target genes)

IT 152406-15-0P 152406-16-1P 152406-19-4P 152406-20-7P 154074-71-2P
155684-96-1P 161140-18-7P 161140-19-8P 161140-20-1P 161140-23-4P
161140-24-5P 161140-25-6P 161247-38-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of immunophilin dimers for regulation of transcription of target genes)

IT 152406-17-2, FK 1012A 152406-18-3, FK 1012B 161140-26-7
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

IT 60-54-8, Tetracycline 53123-88-9, Rapamycin 59865-13-3, Cyclosporin A
79217-60-0, Cyclosporin 104987-11-3, FK506 104987-12-4, FK520
RL: RCT (Reactant)
(regulated transcription of target genes with dimeric ligands which cause chimeric receptor proteins to oligomerize and induce gene transcription)

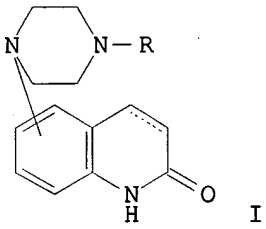
L162 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:161051 HCAPLUS
DN 118:161051
TI carbostyril derivatives as apoptosis regulators for treatment of cancer and other diseases
IN Nakai, Satoru; Aihara, Koutoku; Mori, Hitomi; Tominaga, Michiaki; Adachi, Masakazu; Ichikawa, Hiroyuki; Akamatsu, Seiji; Saito, Fumio
PA Otsuka Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K031-495
CC 1-6 (Pharmacology)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9300902	A1	19930121	WO 1992-JP841	19920702
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 9222317	A1	19930211	AU 1992-22317	19920702
	AU 648690	B2	19940428		
	EP 552373	A1	19930728	EP 1992-914177	19920702 <--

	EP 552373	B1	19991013			
	R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE					
	JP 2628106	B2	19970709		JP 1992-502141	19920702
	ES 2138971	T3	20000201		ES 1992-914177	19920702
	US 5543412	A	19960806		US 1995-469893	19950606
	US 5658912	A	19970819		US 1995-469922	19950606
	US 5672603	A	19970930		US 1995-466449	19950606
	US 5750529	A	19980512		US 1995-469505	19950606
	US 5798356	A	19980825		US 1997-853746	19970509
	US 5872120	A	19990216		US 1997-854074	19970509
	US 5916890	A	19990629		US 1997-854073	19970509
PRAI	JP 1991-162587		19910703			
	JP 1992-33469		19920220			
	JP 1992-45718		19920303			
	JP 1992-100585		19920325			
	WO 1992-JP841		19920702			
	US 1993-989028		19930430			
	US 1995-466449		19950606			

OS MARPAT 118:161051

GI



I

AB Carbostyril derivs. I (R = benzoyl group having lower alkoxy substituents on the Ph ring) or salts thereof are apoptosis regulators effective in treating cancer and other diseases. For example, 6-[4-(3,4-dimethoxybenzoyl)-1-piperazinyl]-3,4-dihydrocarbostyril at 10.mu.g/mL inhibited the growth of leukemia cells in cultures.

ST carbostyril deriv apoptosis regulator cancer; neoplasm inhibitor carbostyril deriv

IT Neoplasm inhibitors
Virucides and Virustats
(carbostyril derivs.)

IT Autoimmune disease
(treatment of, carbostyril derivs. for)

IT Cell aging
(apoptosis, regulators of, carbostyril derivs. as)

IT Blood platelet
(disease, thrombocytopenia, treatment of, carbostyril derivs. for)

IT 81839-51-2 81839-94-3 81840-00-8 81840-15-5 81840-21-3
81849-95-8 81922-74-9 146583-13-3
RL: BIOL (Biological study)
(as apoptosis regulator, for cancer and other disease treatment)

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MOST RECENT DERWENT UPDATE 200131 <200131/DW>
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SEE http://www.derwent.com/covcodes.html <<<

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L201 ANSWER 1 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-258083 [26] WPIX
DNC C2001-077836
TI Use of a composition comprising Mycobacterium phlei-DNA (M-DNA) for the manufacture of medicament to disrupt mitochondrial function in cells to treat e.g. cancer and autoimmune disorders.
DC B04 D16
IN FILION, M C; PHILLIPS, N C
PA (BION-N) BIONICHE LIFE SCI INC
CYC 94
PI WO 2001022979 A1 20010405 (200126)* EN 23p A61K035-74
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001022979 A1 WO 2000-CA1130 20000928
PRAI US 1999-156578 19990929
IC ICM A61K035-74
ICS **A61K031-70**; A61K047-48; A61P035-00; A61P037-00
AB WO 200122979 A UPAB: 20010515
NOVELTY - Use of a composition comprising Mycobacterial phlei (M. pheli)-DNA (M-DNA) for the manufacture of a medicament to disrupt mitochondrial function in cells in the animal, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a composition comprising M-DNA:M. phlei cell wall (MCC) for the manufacture of a medicament to disrupt function in cells in the animal.
ACTIVITY - Antiapoptitic; antiproliferative; antiarthritic; antirheumatic; antidiabetic; antiinflammatory; cytostatic; neuroprotective
Mice were divided into 5 groups. At time 0, the mice in each group received the following: group 1, saline; group 2, MCC in saline; group 3, M-DNA in saline; group 4, Dnase I treated MCC in saline; and group 5, M-DNA in saline. After 2 hours, inflammation was induced in each mouse by the injection of 0.5 ml of a 1% **carrageenan** solution into one hind footpad. Footpad swelling was quantified by measuring water-displacement at 0, 3, 6, 24, 48, 72 and 96 hours after **carrageenan** administration. Groups 2, 3, and 6 mice had less footpad inflammation than groups 1, 4 and 5 mice.
MECHANISM OF ACTION - Mitochondria inhibitor.
USE - M-DNA and MCC are useful for induction of **apoptosis** and inhibition of proliferation, cells include cancer cells and cells implicated in autoreactive, inflammatory and proliferative disorders. Cancer cells include leukemia and breast cancer, autoreactive disorders include multiple sclerosis, rheumatoid arthritis, insulin dependent diabetes mellitus and myasthenia gravis, inflammatory disorders included both acute and chronic inflammation and proliferative disorders include myointimal hyperplasia and T-small lymphocyte disorder.
ADVANTAGE - The use of a composition comprising Mycobacterial phlei (M. phlei)-DNA (M-DNA) is more advantageous than current therapeutic agents to treat disorders that involve aberrant accumulation of unwanted cells, because the composition does not require immune mediators for its activity, it is simple and relatively inexpensive to prepare, its activity

remains therapeutically stable over time and it is effective at dose regimens that are associated with minimal toxicity even upon repeated administration.
Dwg.0/11
FS CPI
FA AB; DCN
MC CPI: B04-E03; B04-F10B2; B14-C03; B14-C09B; **B14-H01**; B14-H01B; B14-J01; B14-S04; D05-H04; D05-H12A
TECH UPTX: 20010515
TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The disruption of mitochondrial function is selected from the disruption of mitochondrial membrane potential, release of cytochrome c into the cytosol and inhibition of the mitochondrial electron transport chain from cytochrome c to cytochrome oxidase. The disruption of mitochondrial function induces a response selected from upregulation of Bax protein expression, degradation of procaspases, activation of caspases, cleavage of cellular substrate targets of activated caspases and release of NuMA, culminating in the inhibition of cell proliferation and the induction of cell **apoptosis**. The cells used are either cancer cells, or cells implicated in autoreactive disorders, inflammatory disorders or proliferative disorders.

L201 ANSWER 2 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-460973 [39] WPIX
DNC C1999-135551
TI Poly-, oligo-, and mono- saccharides used to modulate **apoptosis** - can be used in the treatment of AIDS, cancer and auto-immune diseases.
DC A96 B04
IN ARRIGO, P; CLOAREC, B; CRUZ, F; DESCAMPS, V; RICHARD, C; THIBAL, V; YVIN, J C; YVIN, J
PA (GOEM-N) LAB GOEMAR SA
CYC 84
PI FR 2774289 A1 19990806 (199939)* 26p A61K031-70 <--
WO 9939718 A1 19990812 (199940) FR A61K031-70 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9921710 A 19990823 (200005) A61K031-70 <--
EP 1052996 A1 20001122 (200061) FR A61K031-70 <--
R: DE ES FR GB GR IT NL PT
ADT FR 2774289 A1 FR 1998-1237 19980203; WO 9939718 A1 **WO 1999-FR229 19990203**; AU 9921710 A AU 1999-21710 19990203; EP 1052996 A1 EP 1999-901702 19990203, **WO 1999-FR229 19990203**
FDT AU 9921710 A Based on WO 9939718; EP 1052996 A1 Based on WO 9939718
PRAI FR 1998-1237 19980203
IC ICM **A61K031-70**
ICS **A61K031-715; A61K031-725; A61K035-80**
AB FR 2774289 A UPAB: 19990928
NOVELTY - Medicine comprising, as active ingredient, a substance to modulate disturbances of **apoptosis**.
ACTIVITY - The active ingredients modulate disturbances of **apoptosis**.
MECHANISM OF ACTION - (I9) inhibits Fas **apoptosis**. (L11) potentiates Fas **apoptosis**.
USE - Use to treat disturbances of **apoptosis** is claimed. (I9) can be used for the treatment of AIDS. (L11) can be used for the treatment of cancer and auto-immune diseases.
ADVANTAGE - None given.
Dwg.0/12
FS CPI
FA AB; GI; DCN
MC CPI: A12-V01; B04-C02D; B04-C02X; B10-A07; **B14-G01B**; **B14-G02D**; **B14-H01**

TECH UPTX: 19990928
TECHNOLOGY FOCUS - PHARMACEUTICALS - The active ingredient is at least one polysaccharide, oligosaccharide, or monosaccharide, optionally substituted on one or more of its unit motifs by one or more of sulfate, methyl, and acetyl. The oligosaccharides are derived from 1-3 beta **glucans**, optionally with 1-6 beta branches, or from sulfated galactanes, notably **carrageenans**, **agars**, and **porphyranes**. The oligosaccharide is preferably of formula (I):
n = 1 - 50, preferably 5 - 10;
the number of branches is 0 - 3 per unit of repetition.
The disaccharide is preferably of formula (II):
m = 1 - 50, preferably 1 - 20;
the units of repetition can carry one or more sulfate groups.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The active ingredient is prepared by:
(1) hydrolysis of sodium iota-**carrageenate**, which consists of a mixture of oligo-iota-**carrageenanes** (I9); the total -oses form 62% and the distribution is:
(i) ota-**neocarra-tetraose** (6-8%),
(ii) **hexaose** (23-27%),
(iii) **octaose** (18-22%),
(iv) **decaose** (12-18%),
(v) **dodecaose** (11-15%),
(vi) and oligo-iota-**carrageenanes** consisting of 7-15 disaccharides of repetition (18-22%).
(2) aqueous acid extraction from brown algae, particularly Laminaria digitata, which gives a mixture of 1-3 beta **glucans** (L11) with 1-50, preferably 20-30 saccharidic units.

L201 ANSWER 3 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-337690 [28] WPIX
DNC C1999-099294
TI Compositions comprise 3,6-anhydrogalactopyranose derivative.
DC B02 D13 D21 E13
IN ENOKI, T; IKAI, K; KATO, I; KOYAMA, N; NISHIYAMA, E; SAGAWA, H; SAKAI, T; TOMINAGA, T; YU, F
PA (TAKI) TAKARA SHUZO CO LTD
CYC 83
PI WO 9924447 A1 19990520 (199928)* JA 132p C07H003-10
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9910517 A 19990531 (199941) C07H003-10
EP 1038879 A1 20000927 (200048) EN C07H003-10
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1285838 A 20010228 (200131) C07H003-10
ADT WO 9924447 A1 WO 1998-JP5065 19981111; AU 9910517 A AU 1999-10517 19981111; EP 1038879 A1 EP 1998-953005 19981111, WO 1998-JP5065 19981111; CN 1285838 A CN 1998-813026 19981111
FDT AU 9910517 A Based on WO 9924447; EP 1038879 A1 Based on WO 9924447
PRAI JP 1998-212041 19980713; JP 1997-323917 19971111; JP 1998-20146 19980119; JP 1998-130973 19980427; JP 1998-164410 19980529
IC ICM C07H003-10
ICS A01N001-00; A01N003-00; A23L001-30; A23L003-3544; A23L003-3562; **A61K031-70**; **A61K031-725**; C07H011-00; C08B037-00; C08B037-12; C09K015-06
AB WO 9924447 A UPAB: 19990719
NOVELTY - Medicinal compositions comprise (i) a 3,6-anhydrogalactopyranose (I) or its aldehyde, hydrate or 2-O-methylated derivatives or (ii) a soluble sugar compound containing (i).
DETAILED DESCRIPTION - Medicinal compositions comprise (i) a 3,6-anhydrogalactopyranose (I) of formula (I)

or its aldehyde, hydrate or 2-O-methylated derivatives or (ii) a soluble sugar compound containing (i).

INDEPENDENT CLAIMS are also included for foods, drinks, cosmetics and antioxidants comprising (i) or (ii).

ACTIVITY - Cytostatic. In assays agarobiose had the following IC50 values (no units given) HL-60 (32), Hep2 (8), A-172 (16) and HeLa S3 (8).

MECHANISM OF ACTION - Antioxidant

USE - For inducing **apoptosis**, as active oxygen, lipid peroxide radical and NO radical production inhibitors useful as carcinostatics, antioxidants and preservatives.

ADVANTAGE - The agents have low toxicity and are extracted from natural products (especially algae).

Dwg.0/42

FS CPI

FA AB; GI; DCN

MC CPI: B06-A02; **B14-H01**; B14-S08; D03-H01P; D03-H02E; D08-B; E06-A02E

TECH UPTX: 19990719

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The composition also comprises agar, agarose and/or **carragenan**

L201 ANSWER 4 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1998-322663 [28] WPIX

DNC C1998-099288

TI Butyric ester(s) of poly saccharide(s) for treatment of tumours, etc. - combine anti-proliferative activity of both moieties and improve bio-availability of the butyric residue.

DC A96 B04 B05

IN CORADINI, D; PERBELLINI, A

PA (RICE-N) SOC COOP CENT RICERCHE POLY-TECH A RESPO; (CORA-I) CORADINI D; (PERB-I) PERBELLINI A

CYC 80

PI WO 9823648 A1 19980604 (199828)* EN 34p C08B037-00
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9857515 A 19980622 (199844) C08B037-00
EP 941253 A1 19990915 (199942) EN C08B037-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE SI
IT 1286510 B 19980715 (200053) C12P000-00
US 6140313 A 20001031 (200057) A61K031-72
JP 2001505940 W 20010508 (200131) 34p C08B037-00

ADT WO 9823648 A1 WO 1997-EP6589 19971126; AU 9857515 A AU 1998-57515 19971126; EP 941253 A1 EP 1997-953702 19971126, WO 1997-EP6589 19971126; IT 1286510 B IT 1996-MI2505 19961129; US 6140313 A WO 1997-EP6589 19971126, US 1999-308832 19990525; JP 2001505940 W WO 1997-EP6589 19971126, JP 1998-524276 19971126

FDT AU 9857515 A Based on WO 9823648; EP 941253 A1 Based on WO 9823648; US 6140313 A Based on WO 9823648; JP 2001505940 W Based on WO 9823648

PRAI IT 1996-MI2505 19961129

IC ICM A61K031-72; C08B037-00; C12P000-00
ICS **A61K031-715**; A61P019-00; A61P035-00; A61P043-00

AB WO 9823648 A UPAB: 19980715

Butyric esters (I) of polysaccharides, where the hydroxyl groups are partially or totally esterified with butyric residues and any free hydroxyl groups of the glycosidic residue are optionally esterified with dicarboxylic acid residues, are new.

The polysaccharides are substituted on the carbon atoms of the glycosidic ring by at least 1 group selected from: lower alkyl, NH2, NHCOR, OSO3H, OPO3H2, COOH, COO(CH2)nCOOH, COOR, OR and O(CH2)nOCOR9(n = 1-4 and R = 1-10C alkyl). Free hydroxyls on the glycosidic residue are esterified with at least 1 of 2-9C dicarboxylic acids selected from succinic, tartaric, malic and azelaic acids. (I) contain 0.001-3.0

(preferably 0.01-1.0) hydroxyls esterified with butyric residues per glycosidic monomer and have an average molecular weight of 1 x 104 to 5 x 106. The polysaccharide is a neutral **glucan** containing beta -(1 => 3) and beta -(1 => 6)-glucosidic residues, especially **scleroglucan** or is an anionic polysaccharide containing sulphated and/or carboxylic groups. Preferred anionic polysaccharides include hyaluronic acid, alginic acid, pectin, heparins, heparinoids, **carrageenans** and polysaccharide isolated from Grateloupia doryphora.

USE - (I) combine the known antiproliferative activities of polysaccharides and butyric acid to provide a stable pharmaceutical with a more durable half-life than that of the butyric acid derivatives of the prior art. Both the polysaccharide and the butyric acid moieties are naturally occurring products with anti-proliferative activity and low toxicity. (I) are suitable for the treatment of tumours and conditions susceptible to neoplastic degeneration e.g. inflammatory intestinal diseases, diverticulosis, Crohn's disease and colitis. Similarly (I) can be used to treat disorders caused by synovial cell proliferation and other abnormal cell proliferation e.g. rheumatoid arthritis, psoriasis, hyperkeratosis and prostate hyperplasia. Administration is oral, parenteral, topical or transdermal. Dosage is 0.2-500 mg/kg/day for 1-15 days.

Dwg.0/0

FS CPI
FA AB
MC CPI: A03-A; A10-E07; A12-V01; B04-C02; B14-H01

L201 ANSWER 5 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-172064 [16] WPIX
DNC C1998-055104
TI Cancer therapeutic immune food - comprises U-fucoidan, D-fraction, beta-**glucan**, organic germanium and polysaccharide(s).
DC B04 D13
PA (MATO-I) MATOBA J; (SOGA-I) SOGABE T
CYC 1
PI JP 10033142 A 19980210 (199816)* 4p A23L001-30
ADT JP 10033142 A JP 1996-225814 19960724
PRAI JP 1996-225814 19960724
IC ICM A23L001-30
ICS A61K031-28; A61K031-555; **A61K031-715**; **A61K035-80**; A61K035-84
AB JP 10033142 A UPAB: 19980421
Cancer therapeutic immune food is composed of combinations of several components with different pharmaceutical effects for synergism and acceleration of **apoptosis** and eradication of cancer cells containing U-fucoidan, D-fraction, beta -**glucan**, an organic germanium, and other polysaccharides.

Dwg.0/3

FS CPI
FA AB; DCN
MC CPI: B04-C02; B05-A02; **B14-H01**; B14-S09; D03-H01T2

L201 ANSWER 6 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-082546 [12] WPIX
DNC C1995-037177
TI New water insoluble, cation complexed anionic polysaccharide(s) - used to treat diarrhoea and wt. loss, partic. added to liq. nutritional compsn. as source of dietary fibre, to improve intestinal function without increasing prod. viscosity.
DC A11 A96 B04 C03 D13 D17
IN BARNUM, P E; MAJEWICZ, T G
PA (HERC) HERCULES INC
CYC 23
PI AU 9467502 A 19950127 (199512)* 57p C08B037-06
NO 9402620 A 19950117 (199512) EN C08B037-00
CA 2128160 A 19950117 (199516) C08B037-00

FI 9403296 A 19950117 (199516) C08B037-00
EP 648495 A2 19950419 (199520) EN 35p A61K031-715 <--
R: AT BE CH DE DK ES FR GB IT LI NL PT SE
JP 07090002 A 19950404 (199522) 26p C08B037-00
BR 9402851 A 19950613 (199530) A61K038-16
CZ 9401702 A3 19951018 (199549) C08B037-00
EP 648495 A3 19950809 (199613) C08B037-06
NZ 260933 A 19960726 (199635) A23L001-052
AU 675542 B 19970206 (199714) C08B037-06
CN 1104890 A 19950712 (199729) A61K031-715 <--
HU 75240 T 19970528 (199803) A61K031-715 <--
EP 648495 B1 20000105 (200006) EN A61K031-715 <--
R: AT BE CH DE DK ES FR GB IT LI NL PT SE
DE 69422465 E 20000210 (200015) A61K031-715 <--
ES 2140482 T3 20000301 (200018) A61K031-715 <--

ADT AU 9467502 A AU 1994-67502 19940715; NO 9402620 A NO 1994-2620 19940712; CA 2128160 A CA 1994-2128160 19940715; FI 9403296 A FI 1994-3296 19940711; EP 648495 A2 EP 1994-111053 19940715; JP 07090002 A JP 1994-163665 19940715; BR 9402851 A BR 1994-2851 19940718; CZ 9401702 A3 CZ 1994-1702 19940714; EP 648495 A3 EP 1994-111053 19940715; NZ 260933 A NZ 1994-260933 19940705; AU 675542 B AU 1994-67502 19940715; CN 1104890 A CN 1994-116163 19940716; HU 75240 T HU 1994-2102 19940714; EP 648495 B1 EP 1994-111053 19940715; DE 69422465 E DE 1994-622465 19940715, EP 1994-111053 19940715; ES 2140482 T3 EP 1994-111053 19940715

FDT AU 675542 B Previous Publ. AU 9467502; DE 69422465 E Based on EP 648495; ES 2140482 T3 Based on EP 648495

PRAI US 1993-93231 19930716

REP No-SR.Pub; EP 191572; EP 29724; EP 40048; EP 483070; EP 506563; FR 2073254; FR 7686; US 3474086; US 5104677; WO 8704350; WO 9104674; WO 9319613; WO 9325096

IC ICM A23L001-052; **A61K031-715**; A61K038-16; C08B037-00; C08B037-06
ICS A23L001-0524; A23L001-0526; A23L001-29; A23L001-305; A23L001-308; A23L001-48; A23L002-52; A61K009-10; A61K031-195; **A61K031-70**; **A61K031-725**; A61K031-74; A61K038-00; C08B011-00; C08B011-12; C08B015-00; C08B031-00; C08B031-12; C08B037-04; C08L001-08; C08L003-04; C08L005-00

ICI A61K031-725, A61K031:195, A61K033:06, A61K033:14; A61K031-725, A61K033:06, A61K033:14

AB AU 9467502 A UPAB: 19950328

Water-insoluble, cation-complexed anionic polysaccharides (I) are new.

The cation is at least one alkali, alkaline earth or transition metal, esp. Ca, Fe, Mg, Zn, K, Na, Al, Cu and/or Mn.

The polysaccharide is (a) carboxylated, i.e. an alginate, pectin, gum (arabic, karaya, tragacanth, ghatti, psyllium, xanthan or gellan), flaxseed, okra, carboxymethylated cellulose, guar or starch, or hyaluronic acid; (b) sulphated, i.e. **carrageenan**, heparin, keratan or chondroitin, dermatan, heparin, keratan or cellulose sulphates, or (c) phosphated cellulose, starch or **glucan**. Partic. the polysaccharide is a pectin of methyl or acetyl esterification below 5 % and degree of polymerisation over 150, esp. complexed with Ca at mole ratio Ca; anhydrogalacturonic acid 0.1-0.6.

USE - (I) have an antidiarrhoeal effect in humans and other animals, partic. in subjects who have undergone surgery for removal of part of the gastrointestinal tract, but also in e.g. diabetes, cardiovascular disease, cancer, AIDS etc. They can also be used to treat wt. loss.

Partic. (I) are incorporated into foods (e.g. liq. feeding compsns.) or pharmaceutical compsns.

ADVANTAGE - (I) is a source of dietary fibre that can be incorporated into liq. or solid feeding compsns. for oral or enteral delivery. It improves gastrointestinal function (nutrient and water absorption) without increasing the viscosity of liq. formulations (even after heat sterilisation) and with no significant effect on flavour, colour or coagulation behaviour.

Dwg.0/0

FS CPI

FA AB; DCN
MC CPI: A03-A01; A12-V01; B04-C02A; C04-C02A; B04-C02B; C04-C02B; B04-C02D; C04-C02D; B04-C02E; C04-C02E; B14-E02; C14-E02; D03-H01T1; D06-H

L201 ANSWER 7 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-082796 [10] WPIX
DNN N1994-064763 DNC C1994-037859
TI Treating or preventing irritable bowel syndrome - by orally administering an anion-binding and hydrophilic polymer eg colestipol and pectin.
DC A96 B04 P34
IN DAY, C E
PA (DAYC-I) DAY C E
CYC 43
PI WO 9404136 A1 19940303 (199410)* EN 27p A61K009-58
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR CA CZ FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD SK UA
AU 9347978 A 19940315 (199428) A61K009-58
US 5380522 A 19950110 (199508) 6p A61K031-74
EP 654992 A1 19950531 (199526) EN A61K009-58
R: DE FR GB NL
CN 1085084 A 19940413 (199527) A61K031-725 <--
AU 667955 B 19960418 (199623) A61K031-74
IL 106640 A 19970415 (199726) A61K047-00
ADT WO 9404136 A1 WO 1993-US7242 19930802; AU 9347978 A AU 1993-47978 19930802; US 5380522 A US 1992-928509 19920811; EP 654992 A1 EP 1993-918568 19930802, WO 1993-US7242 19930802; CN 1085084 A CN 1993-116222 19930811; AU 667955 B AU 1993-47978 19930802; IL 106640 A IL 1993-106640 19930810
FDT AU 9347978 A Based on WO 9404136; EP 654992 A1 Based on WO 9404136; AU 667955 B Previous Publ. AU 9347978, Based on WO 9404136
PRAI US 1992-928509 19920811
REP 1.Jnl.Ref; US 3579634; US 3627872; US 3974272; US 4172120; US 4303638; US 4895723; US 4999341; US 5026555; US 5102664; US 5112856; US 5213806
IC ICM A61K009-58; **A61K031-725**; A61K031-74; A61K047-00
ICS A01N043-04; A61K009-68; A61K031-35; A61K031-47; **A61K031-70**; **A61K031-715**; A61K031-785; A61K039-02; A61L009-04
AB WO 9404136 A UPAB: 19940421
An orally ingestible pharmaceutical compsn. consists of a dry powdered admixture of an anion-binding polymer and a hydrophilic polymer, or a polymer which is both an anion-binding polymer and a hydrophilic polymer, opt. together with a suitable diluent or carrier. A method of treating or preventing irritable bowel syndrome, including diarrhoea, constipation and pain associated with the syndrome, in a human, consists essentially of orally administering an anion-binding polymer and a hydrophilic polymer either simultaneously, concurrently or in the above form.

The anion-binding polymer is pref. cholestyramine, a colestipol acid-addition salt MCI-196 or diethylaminoethyl dextran and the hydrophilic polymer is pectin, guar gum, psyllium hydrophilic colloid, locust bean gum, alginic acid, cellulose gum, **carrageenan**, oat bran beta-glutan, xanthan gum, methylcellulose or polycarbophil, pref. respectively cholestyramine or a colestipol salt and pectin, or the two characteristics are combined in a single polymer, esp. chitosan.

The total amt. of polymer per dose of the compsn. is suitably 1-24g.
Dwg.0/0
FS CPI GMPI
FA AB; DCN
MC CPI: A12-V01; B04-C02; B04-C03B; B14-E02; B14-E10
ABEQ US 5380522 A UPAB: 19950301
Treating irritable bowel syndrome including diarrhoea, constipation and pain or their symptoms in humans comprises oral admin of an anion-binding polymer (ABP) and a hydrophilic polymer (HP) simultaneously or concurrently or in the form of a compsn.

Pref the wt. ratio of ABP to HP is 2:1 to 1:2 ABP is eg cholestyramine cholestypol or diethylamino dextran and HP is e.g. pectin, psyllium hydrophilic colloid, cellulose gum, algine acid, methyl

cellulose, polycarbophil, locust bean gum, carrogeenan, xanthan gum or oat bran beta-**glucan**.

ADVANTAGE - There was previously no effective treatment for irritable bowel syndrome.

Dwg.0/0

L201 ANSWER 8 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-182688 [22] WPIX
CR 1991-325347 [44]; 1994-150866 [18]
DNN N1993-140406 DNC C1993-080972
TI Contrast medium for diagnostic imaging - comprises gel particles of less than 90 microns in mean dia. and which comprise a polymer entrapping a contrast enhancing metal.
DC A96 B04 P31 S03 S05
IN UNGER, E C
PA (UNGE-I) UNGER E C; (IMAR-N) IMARX PHARM CORP
CYC 20
PI WO 9310440 A1 19930527 (199322)* EN 43p G01N024-08
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: AU CA JP
AU 9228940 A 19930615 (199340) G01N024-08
EP 614527 A1 19940914 (199435) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
US 5358702 A 19941025 (199442) 13p A61B005-055
JP 07501331 W 19950209 (199515) A61K049-00
AU 667491 B 19960328 (199622) A61K049-04
US 5976500 A 19991102 (199953) A61B005-055
ADT WO 9310440 A1 WO 1992-US8948 19921020; AU 9228940 A AU 1992-28940 19921020; EP 614527 A1 EP 1992-922870 19921020, WO 1992-US8948 19921020; US 5358702 A CIP of US 1990-507125 19900410, Cont of US 1991-794437 19911119, US 1993-62325 19930514; JP 07501331 W WO 1992-US8948 19921020, JP 1993-509251 19921020; AU 667491 B AU 1992-28940 19921020; US 5976500 A CIP of US 1990-507125 19900410, Cont of US 1991-794437 19911119, Div ex US 1993-62325 19930514, US 1994-285977 19940804
FDT AU 9228940 A Based on WO 9310440; EP 614527 A1 Based on WO 9310440; JP 07501331 W Based on WO 9310440; AU 667491 B Previous Publ. AU 9228940, Based on WO 9310440; US 5976500 A Div ex US 5358702
PRAI US 1991-794437 19911119; US 1990-507125 19900410; US 1993-62325 19930514; US 1994-285977 19940804
REP US 4452773; US 4692325; US 4735796; US 4749560; US 4863715; US 4985233; US 5128121; US 5160725
IC ICM A61B005-055; A61K049-00; A61K049-04; G01N024-08
ICS A61K009-16; **A61K031-715**; A61K047-30
AB WO 9310440 A UPAB: 19991215
Contrast medium comprises gel particles of less than 90 microns in mean diameter. The gel particles comprise a polymer entrapping a contrast enhancing metal.

Also claimed are (1) a contrast medium of gel particles which comprise a non-crosslinked polymer entrapping a contrast enhancing metal; (2) a method of providing an image of an internal region of a patient, or for diagnosing the presence of diseased tissue in a patient, comprises: (i) administering to the patient a contrast medium as described in (A) or (B) above, and (ii) scanning the patient using magnetic resonance imaging, ultrasound imaging X-ray imaging to obtain visible images of the region or of any diseased galacturonans, **glucans**, mannans, xylans, levan, fucoidan, **carrageenan**, galactocarolose, pectins, pectic acids, amylose, pullulan, glycogen, amylopectin, cellulose, dextran, pustulan, chitin, agarose, keratin, chondroitin, dermatan, hyaluronic acid, alginic acid, xanthan gum, starch, carboxymethyl cellulose, hydroxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, methoxycellulose, and polysaccharides contg. an aldose, ketose, acid or amine selected from erythrose, threose, ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, tabose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, glucuronic acid, gluconic acid, **glucanic** acid, galacturonic acid, mannuronic acid, glucosaminae galactosamine and neuraminic acid.

Pref. the polysaccaride is pectin which is a low methoxy pectin having phosphorylated 30% methoxylation, polygalacturonic acid or the polymer may be a phosphorylated polymer
Dwg.0/1
Dwg.0/1
FS CPI EPI GMPI
FA AB; DCN
MC CPI: A12-V03C2; A12-V03D; B04-C02; B04-C03B; B04-C03D; B05-A03; B11-C08A; B12-K04C; B12-K07; B12-M03
EPI: S03-E07A; S03-E09X; S05-D02B2
ABEQ US 5358702 A UPAB: 19941212
Pharmaceutically acceptable contrast medium comprises firm gel particles of less than 90 microns mean dia. The particles comprise at least one methoxylated natural or modified natural polymer entrapping contrast enhancing material.
Pref. dia. of gel particles in 5 nm- 90 micron (10-200)nm. Pref. polymer is a polysaccharide.
USE - As contrast medium for X-ray, ultra-sound and MRI imaging.
Dwg.0/1

L201 ANSWER 9 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1982-89076E [42] WPIX
TI Hypoglycaemic compsn. for treating metabolic and digestive diseases - comprise difficult to digest polysaccharide(s), oligosaccharide(s) or their derivs..
DC B04 D16
PA (ENDO-I) ENDO A
CYC 1
PI JP 57146713 A 19820910 (198242)* 4p
PRAI JP 1981-33513 19810309; JP 1983-186305 19810309
IC **A61K031-70**; C07H003-06
AB JP 57146713 A UPAB: 19930915
Hypoglycemics contain, as active ingredient, saccharides selected from hardly digestable polysaccharides, oligosaccharides and their derivs., which are pref. those produced by microorganisms or those obtd. from vegetables or animals.
Hardly digestable polysaccharides of microorganism origin include alpha-**glucans** (e.g. dextran, erucinan), beta-**glucans** (e.g. cellulose, sclerotan), and polysaccharides produced by bacteria of the genus Azotobacter, Pseudomonas, Rhinocladiella, Cryptococcus, etc. Hardly digestable polysaccharides of vegetable or animal origin include cellulose, hydroxyethyl starch, mannan, pectin, guar gum, **carragheenin**, chitosan, etc. Hardly digestable oligosaccharides of bacterium origin include alpha-, beta- and gamma-cyclodextrin, isomaltotriose, isomaltotetrose, isomaltopentose, etc.
Acute toxicity at least 500 mg/Kg (p.o.) Dosage is 0.1-10 g/day, pref. 0.2-5 g/day, orally.
FS CPI
FA AB
MC CPI: B04-C02; B12-H05; B12-J01; D06-H

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=> d his

(FILE 'HOME' ENTERED AT 09:26:49 ON 13 JUN 2001)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:27:03 ON 13 JUN 2001
E WO99-FR229/AP,PRN
L1 1 S E3,E4
E FR99-1237/AP,PRN
E FR98-1237/AP,PRN
L2 1 S E3,E4

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L3            1 S L1,L2
                E YVIN J/AU
L4           37 S E4,E5
                E CRUZ F/AU
L5           77 S E3-E12,E31
                E DESCAMPS V/AU
L6           10 S E3,E4
                E RICHARD C/AU
L7          202 S E3-E15,E39-E40
                E THIBAL V/AU
L8            1 S E4
                E ARRIGO P/AU
L9           11 S E3,E4
                E CLOAREC B/AU
L10           5 S E4
                E GOEMAR/PA,CS
L11          33 S E3-E9
L12         334 S L4-L11
L13           1 S L3 AND L12
                E APOPTOSIS/CW
L14       30798 S E3
                E APOPTOSIS/CT
                E E3+ALL
L15        1048 S E5
L16       43760 S E4/BI,CT
                E E3+ALL
L17       34377 S E3+NT
L18        1483 S E4
L19       17461 S E9+NT OR E8+NT OR E10+NT OR E11+NT OR E12+NT
L20       62340 S L14-L19
L21           3 S L12 AND L20
L22           1 S L21 AND ?SACCHARID?
L23           1 S L13,L22
L24          23 S L12 AND ?SACCHARID?
L25           6 S L12 AND CARBOHYDRATE#/SC,SX
                E SACCHARIDE/CW
L26        1039 S E4
                E MONOSACCHARIDE/CW
L27        6883 S E3,E4
                E DISACCHARIDE/CW
L28        1103 S E4
                E TRISACCHARIDE/CW
L29         234 S E4
                E POLYSACCHARIDE/CW
L30       32500 S E3,E4
                E OLIGOSACCHARIDE/CW
L31       22161 S E3,E4
                E OLIGOSACCHARIDE/CT
                E E9+ALL
L32        1040 S E4,E5
L33      122473 S E3+NT
L34      174616 S ?SACCHARID?
L35        4891 S BETA(2W)GLUCAN
L36           3 S IOTA()NEOCARRATETRAOSE
L37           3 S IOTA()NEOCARRAHEXAOSE
L38           1 S IOTA()NEOCARRAOCTAOSE
L39           1 S IOTA()NEOCARRADECAOSE
L40           1 S IOTA()NEOCARRADODECAOSE
L41         763 S IOTA()CARRAGEENAN
L42           0 S OLIGO(L)IOTA()CARRAGEENAN
L43           1 S OLIGO(L)IOTA(L)CARRAGEENAN
L44           6 S OLIGO(L)CARRAGEENAN
L45          11 S NEOCARRATETRAOSE OR NEOCARRAHEXAOSE OR NEOCARRAOCTAOSE OR NEO
L46           0 S NEO(L)(CARRATETRAOSE OR CARRAHEXAOSE OR CARRAOCTAOSE OR CARRA
L47          12 S ?CARRATETRAOSE OR ?CARRAHEXAOSE OR ?CARRAOCTAOSE OR ?CARRADEC
L48          12 S ?CARRATETRAOS? OR ?CARRAHEXAOS? OR ?CARRAOCTAOS? OR ?CARRADEC
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     FILE 'REGISTRY' ENTERED AT 09:42:08 ON 13 JUN 2001
L49           1 S 9062-07-1
L50           5 S 237069-70-4 OR 237069-74-8 OR 237069-76-0 OR 237069-79-3 OR 2
L51           0 S (237069-70-4 OR 237069-74-8 OR 237069-76-0 OR 237069-79-3 OR

     FILE 'HCAPLUS' ENTERED AT 09:43:45 ON 13 JUN 2001
L52           1 S L50
L53          12 S L36-L40,L45,L47,L48,L52
L54           1 S L53 AND L20
L55           2 S L53 AND L35
L56           4 S L53 AND L41
L57           5 S L23,L54-L56
L58           1 S L57 AND (1 OR 63)/SC,SX

     FILE 'REGISTRY' ENTERED AT 09:47:51 ON 13 JUN 2001
L59           1 S 11016-36-7
L60           1 S 9002-18-0
L61           1 S 9000-07-1
L62           1 S 39475-64-4
                E L-GALACTAN/CN
L63           1 S E3
                E D-GALACTAN/CN
L64           1 S E3
                E DL-GALACTAN/CN
L65           2 S L63,L64
                SEL RN
L66           7 S E1-E2/CRN
L67           1 S L66 AND H2O4S AND 2/NC

     FILE 'HCAPLUS' ENTERED AT 09:49:52 ON 13 JUN 2001
L68        6986 S L59 OR L60 OR L61 OR L62 OR L67 OR L65
L69       47922 S CARRAGEENAN OR AGAR OR PORPHYRAN OR GALACTAN (A) (SULFATE? OR
L70         253 S L69 AND L20
L71           1 S L70 AND L53
L72          20 S L68 AND L20
L73           1 S L72 AND L53
L74           1 S L71,L73,L58
L75         940 S BETA 1 3 GLUCAN

     FILE 'REGISTRY' ENTERED AT 09:55:08 ON 13 JUN 2001
L76           1 S 9051-97-2
L77           1 S 54724-00-4
                E BETA.-DL-GLUCAN/CN
                E BETA.-L-GLUCAN/CN
                E BETA.-D-GLUCAN/CN
                E .BETA.-D-GLUCAN/CN
L78           2 S E49
                E .BETA.-DL-GLUCAN/CN
                E .BETA.-L-GLUCAN/CN

     FILE 'HCAPLUS' ENTERED AT 09:57:29 ON 13 JUN 2001
L79        1577 S L78
L80           5 S L79 AND L20
L81           3 S L80 AND APOPTO?
L82           2 S L80 AND CELL()(DEATH OR SURVIV? OR AGING OR AGEING)
L83           4 S L81,L82,L74
L84        5171 S BETA (3W) GLUCAN
L85        5171 S L75,L84
L86        1957 S L85 AND 1 3
L87          12 S L86 AND L20
L88           3 S L87 AND APOPTO?
L89           5 S L87 AND CYTOL?
L90          10 S L83,L88,L89
L91           2 S L90 AND (FUNGAL OR YEAST)/TI
L92           8 S L90 NOT L91
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     FILE 'REGISTRY' ENTERED AT 10:08:16 ON 13 JUN 2001
L93            1 S 9062-07-1

     FILE 'HCAPLUS' ENTERED AT 10:08:34 ON 13 JUN 2001
L94          739 S L93
L95          763 S IOTA CARRAGEENAN
L96          854 S L94,L95
L97            3 S L20 AND L96
L98           27 S L20 AND L85
L99           10 S L92,L97
L100           2 S L99 NOT L92
L101           8 S L99 NOT L100
                 E FAS LIGAND/CT
                 E E3+ALL
L102        2086 S E6,E5+NT
                 E E10+ALL
L103        3739 S E7,E6+NT
L104        4371 S L102,L103
L105           1 S L104 AND L53
L106           1 S L104 AND L79,L85,L96
L107           8 S L101,L105,L106
L108        5715 S L79,L85
L109        5715 S BETA (S) GLUCAN
L110        6212 S L108,L109
L111          83 S L110 AND L68
L112         118 S L110 AND L69
L113         140 S L111,L112
L114           6 S L113 AND L96
L115          18 S L113 AND 63/SC,SX
L116          21 S L113 AND 1/SC,SX
L117           5 S L113 AND 15/SC,SX
L118          22 S L113 AND THU/RL
L119          38 S L115-L118
L120          35 S L119 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L121           8 S L120 AND (ANTITUMOR OR SSG OR BRANCHED OR BOWEL OR CONFORMATI
L122           7 S  L121 NOT BOWEL/TI
L123          15 S L92,L101,L107,L122

     FILE 'REGISTRY' ENTERED AT 10:28:08 ON 13 JUN 2001
L124           1 S 9041-22-9

     FILE 'HCAPLUS' ENTERED AT 10:28:18 ON 13 JUN 2001
L125           1 S L124 AND L123
L126          15 S L123,L125
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 10:29:02 ON 13 JUN 2001
L127          13 S E1-E13

     FILE 'HCAPLUS' ENTERED AT 10:29:24 ON 13 JUN 2001
L128       43760 S L14-L16
L129       45691 S APOPTO?
L130       45691 S L128,L129
L131       18470 S L20 NOT L130
L132          54 S OLIGOSACCHARID? AND L130
L133          97 S OLIGOSACCHARID? AND L131
L134         150 S L132,L133 NOT L126
L135         128 S L134 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L136           0 S L135 AND GLUCAN
L137           0 S L135 AND POLYGLUCAN
L138           1 S L135 AND ?CARRAGEEN?

     FILE 'MEDLINE' ENTERED AT 10:31:58 ON 13 JUN 2001
                 E APOPTOSIS/CT
                 E E3+ALL
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L139       34434 S E5+NT
L140       42347 S E5,E7/BI
                 E APOPTO
L141       42333 S E37
L142       16893 S E51
L143          18 S E61-E63
L144       44190 S L140-L143
                 E OLIGOSACCHARIDE/CT
                 E E5+ALL
L145       44089 S E5+NT
L146      241469 S E4+NT
L147        1647 S BETA (3W) GLUCAN
                 E GLUCANS/CT
                 E E3+ALL
L148        2464 S E5
L149        2811 S E5/BI,CN
L150           0 S L124
L151           0 S L93
L152         429 S L76-L78
L153           0 S L49
L154           0 S L50
L155           8 S L36-L40,L43-L45,L48
L156         797 S L144 AND L145-L155
L157          13 S L156 AND ?GLUCAN?
L158           9 S L157 AND PY<=1999

     FILE 'HCAPLUS' ENTERED AT 10:40:43 ON 13 JUN 2001

     FILE 'REGISTRY' ENTERED AT 10:41:25 ON 13 JUN 2001

     FILE 'MEDLINE' ENTERED AT 10:42:00 ON 13 JUN 2001

     FILE 'HCAPLUS' ENTERED AT 10:42:34 ON 13 JUN 2001
                 E WO9502684/PN
L159           2 S E3
                 E EP0552373/PN
L160           1 S E3
                 E EP0795560/PN
L161           1 S E3
L162           4 S L159-L161 NOT L126

     FILE 'HCAPLUS' ENTERED AT 10:44:25 ON 13 JUN 2001

     FILE 'WPIX' ENTERED AT 10:45:42 ON 13 JUN 2001
                 E WO99-FR229/AP,PRN
L163           1 S E3
L164       11411 S A61K031-70/IC
L165        1747 S A61K031-715/IC
L166         903 S A61K031-725/IC
L167         499 S A61K035-80/IC
L168          43 S L167 AND L164-L166
                 E R24036+ALL/DCN
L169         309 S E1
                 E R24070+ALL/DCN
L170         417 S E1
                 E CARRAGEEN
L171        2223 S E2,E5,E6,E8-E11
L172         376 S E13-E21,E23,E24
L173          24 S E25,E28-E36
L174         110 S E39-E48
L175         127 S E49-E60
L176          35 S E61-E64,E66-E72
L177          49 S E73-E80
                 E CARAGE
L178           1 S E4
L179        2665 S ?CARRAGEEN?
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L180       3048 S L169,L171-L179
L181         33 S L180 AND (GLUCAN OR POLYGLUCAN)
L182          1 S L181 AND ?NEOCARRA?

     FILE 'WPIX' ENTERED AT 10:58:33 ON 13 JUN 2001
L183          1 S L181 AND (TETRAOSE OR ?HEXAOSE OR ?OCTAOSE OR ?DECAOSE OR ?DO
L184          1 S L181 AND PORPHYRAN?
L185         13 S L181 AND AGAR
L186          5 S L181 AND L170
L187         13 S L182-L186
L188          3 S APOPTO? AND L180
L189        147 S APOPTO? AND L164-L167
L190          2 S L189 AND (GLUCAN OR POLYGLUCAN)
L191          4 S L188,L190
L192         83 S L189 AND (B14-H01 OR C14-H01 OR B12-G07 OR C12-G07 OR B14-G01
L193         98 S L189 AND (P633 OR P434 OR P210)/M0,M1,M2,M3,M4,M5,M6
L194          2 S L192,L193 AND  ?GLUCAN?
L195          4 S L163,L182,L191,L194
L196          4 S L195 AND L163-L194
L197        182 S ?GLUCAN? AND L164-L167
L198          6 S L197 AND L180
L199          5 S L198 NOT L196
L200          9 S L196,L198-L199
L201          9 S L200 AND L163-L199

     FILE 'WPIX' ENTERED AT 11:06:56 ON 13 JUN 2001
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